Archives of Neurology and Psychiatry

VOLUME 58 DECEMBER 1947 NUMBER 6

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CENTRAL NERVOUS SYSTEM IN PNEUMONIA (NONSUPPURATIVE PNEUMONIC ENCEPHALITIS)

III. An Experimental Study

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THE CEREBRAL complications associated with pneumonia have received but scant attention in American literature, although numerous reports are available in many of the foreign journals (Bonaba, Marcos and de Agorio [1]; Comby [2]; Bonaba, Boni and Barberouse [3]; de Filippi and Fernández [4]; Nové-Josserand and associates [5]; Gareiso and Sagreras [6]; Mollard and Dufourt [7]; Eschbach [8]; Stephan [9]; Comby [10]). Actually, such complications are not infrequent and may appear at the onset or at the height of the pneumonia or during convalescence, after the patient has become afebrile and appears well along the road to recovery. Cases often reveal a wide variability of symptoms,

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This study was aided by a grant from the John and Mary Markle Foundation.

1. Bonaba, J.; Marcos, J. R., and Mendivil de Agorio, S.: Nuevos casos de encefalitis neumónica, Arch. de pediat. d. Uruguay **12**:317, 1941.

2. Comby, J.: L'encéphalite aiguë chez les enfants, Arch. de méd. d. enf. **10**:577, 1907.

3. Bonaba, J.; Boni, E., and Barberouse, C. M.: Tres nuevos casos de encefalitis post-neumónica, Arch. de pediat. d. Uruguay **8**:245, 1937.

4. de Filippi, F., and Fernández, I.: Encefalitis paraneumónica, Arch. argent. de pediat. **11**:22, 1939.

5. Nové-Josserand, L.; Rougier, and Feuillade: Névraxite consécutive à une pneumonie chez une enfant de 4 ans; guérison, Lyon méd. **153**:272, 1934.

6. Gareiso, A., and Sagreras, P. O.: Encefalitis agudas en los procesos infecciosos, Rev. argent. de neurol. y psiquiat. **2**:233, 1936.

7. Mollard, J., and Dufourt, A.: Sur l'encéphalite aiguë au cours de la pneumonie, Lyon méd. **66**:821, 1911.

8. Eschbach, H.: Pneumopathies à manifestations cérébro-méningées, Arch. méd.-chir. de Province **27**:47, 1937.

9. Stephan, B. H.: Des paralysies pneumoniques, Rev. de méd., Paris **9**:60, 1889.

10. Comby, M.: Les encéphalites aiguës post-infectieuses de l'enfance, Thesis, Paris, Masson & Cie, 1935.

ranging from such generalized complaints as headache, vomiting, vertigo and lethargy to the more dramatic complications of coma, convulsions, delirium, monoplegia, hemiplegia, athetoses and psychic disturbances (Baker and Noran [11]). The most common picture seen is that of acute meningoencephalitis. In many instances, after a short period of generalized symptoms, a severe delirium or convulsions of a focal or generalized nature may develop (Mollard and Dufourt,[7] Reimann,[12] Stephan,[9] Comby,[2] Eschbach,[8] Garzón [13]). Since these cerebral complications generally appear at the height of the illness or at the time the acute infectious process is subsiding, they have been suspected of being merely the result of a toxic condition or of pyrexia.

Significant cerebral complications of pneumonia, however, may occur a few days to a few weeks after the patient's temperature has returned to normal, at a period when recovery would seem inevitable. There is generally a dramatic and abrupt onset of lethargy and stupor, often associated with focal motor symptoms. The severity of the pneumonic process plays no part in the incidence of these complications. Recovery is usually delayed and improvement is slow, often leaving permanent sequelae.

In an attempt to investigate the nature of the resulting cerebral changes, the nervous system in 10 fatal cases was studied in detail (Noran and Baker [14]). It was observed that the pathologic alterations were similar in each case regardless of the etiologic agent causing the pneumonia. The changes varied only in degree and severity. The cerebral lesions consisted primarily of thrombi or intravascular clots and petechial hemorrhages. In the milder cases many of the smaller vessels were partially or completely occluded by homogeneous material, within which special stains often revealed interlacing strands of fibrin. In the cases of severer involvement this vascular thrombosis or clotting was more extensive, implicating a relatively large percentage of the vessels. Blood vessels of all sizes were partially or completely occluded by these clots. Mild hemorrhagic lesions were not infrequent, and vascular congestion was prominent. Many of the smaller occluded

11. Baker, A. B., and Noran, H. H.: Changes in the Central Nervous System Associated with Encephalitis Complicating Pneumonia: I. A Clinical Study, Arch. Int. Med. **76**:146 (Sept.) 1945.

12. Reimann, H. A.: An Acute Infection of the Respiratory Tract with Atypical Pneumonia: A Disease Entity Probably Caused by a Filtrable Virus, J. A. M. A. **111**:2377 (Dec. 24) 1938.

13. Garzón, W. P.: Meningoencefalitis postneumónica, Med. de los niños **35**:261, 1934.

14. Noran, H. H., and Baker, A. B.: The Central Nervous System in Pneumonia (Nonsuppurative Pneumonic Encephalitis): II. A Pathologic Study, Am. J. Path. **22**:579, 1946.

vessels were surrounded by a zone of erythrocytes or by areas of mild perivascular demyelination. In the 10 cases studied the etiologic agents causing the pneumonia were variable, including a nonhemolytic streptococcus, a staphylococcus and a type III pneumococcus, and in several cases the disease was the so-called virus pneumonia. Probably the most remarkable case was that of encephalitis following a typical lipid pneumonia, the presence of which was confirmed by fat stains. The fact that the cerebral lesions were similar regardless of the etiologic agent or process causing the pneumonia suggested that they were probably produced by some product of the injured lung tissue rather than by an infectious agent.

In an attempt to produce experimentally the lesions of pneumonia encephalitis, various animals were inoculated intravenously and intra-arterially with the filtrate of homogenized lung tissue. It soon became apparent that all animals were extremely sensitive to intravenous inoculation of small amounts of "homologous" lung extract, that is, an extract of lung tissue of the same species of animal. Heterologous extracts (extracts of lung tissue of a different animal species) had little or no effect on the animal, even when given in much larger amounts. For example, from 0.5 to 1 cc. of a 1:25 dilution of rabbit lung extract when given intravenously was fatal to most rabbits in thirty seconds to two minutes. Extracts of lung tissue of the guinea pig, sheep, dog and hog were essentially harmless to a rabbit, even when given in larger doses, but was fatal to the same species of animal. It was also observed that this curious action was highly specific for lung tissue only. Intravenous injection of large doses of homologous extracts of other organs, such as brain, liver, kidney, intestine and spleen, produced no untoward effects (Baker, Noran and Larson [15]).

It was discovered that the harmful effects of homologous lung extract could be prevented by a preliminary intravenous injection of 10 mg. of heparin, indicating that the reactions were due to some effect on the clotting mechanism. Lung tissue extract which had been heated at 56 C. for thirty minutes proved inactive, suggesting that the active principle within the lung tissue was thermolabile and probably contained thrombin.

It would appear, therefore, that in homogenizing lung tissue to prepare the extract thromboplastin was liberated. This substance would probably react with the prothrombin of the lung, causing the development of thrombin. This thrombin apparently is the active principle in the lung extract producing the precipitation of fibrin when inoculated

15. Baker, A. B.; Noran, H. H., and Larson, W. P.: Clotting of Blood in Vivo by Aqueous Homologous Lung Extract: Some Clinical Implications, Proc. Soc. Exper. Biol. & Med. **59**:196, 1945.

intravenously. From our studies, it would seem that in some cases of pneumonia the breakdown of the lung tissue results in a similar process, that is, in the liberation of thromboplastin, which initiates the mechanism of blood clotting, to result in plugs of fibrin within the cerebral vessels.

EXPERIMENTAL INVESTIGATION

METHOD

In order to throw further light on the morphologic character of the cerebral alterations associated with pneumonia, the brains of the experimental animals were studied pathologically. Thirty-one experimental animals, including rabbits, guinea pigs and dogs, were available. In many of the animals the tissue changes were necessarily acute, since the animals died immediately after inoculation with the lung extract. However, it was observed that smaller doses of the extract were frequently not fatal. Such sublethal inoculations were given to many animals in an attempt to produce a more chronic involvement of the brain. The response of the animals, however, was not consistent, since a few survived inoculation of as much as 1 cc. of the extract, while others died quickly after injection of as little as 0.25 cc. The brains of all the experimental animals were sectioned and prepared for microscopic study with the following staining technics: the routine phloxine-hematoxylin stain, the cresyl violet stain for Nissl bodies, the Weil stain for myelin sheaths, the Bodian stain for axis-cylinders, the Mallory-Heidenhain stain for connective tissue, the Alzheimer-Mann stain for astrocytes and the Mallory phosphotungstic acid hematoxylin stain. Nineteen of the experimental animals were rabbits, 5 were guinea pigs, and 7 were dogs.

RABBITS

The 19 rabbits were divided into four experimental groups. For the sake of convenience, these experiments were termed acute, subacute, subacute to chronic and chronic. A 1:25 saline dilution of extract of finely homogenized lung tissue from a rabbit was injected intravenously in all animals. In the acute experiments the animals died either immediately or within four or five hours after the inoculation of lung extract. When the animal lived more than one day or as long as two or three days, the experiment was arbitrarily termed subacute. All the rabbits of the subacute groups received two or more intravenous inoculations. In the subacute to chronic experiments the duration was six to twelve days. When several injections of the lung extract were given over a longer period, the experiment was regarded as chronic.

Acute Experiments.—Four rabbits were included in this study. Two had convulsions and died immediately after the intravenous inoculation of 1 cc. of homologous lung extract. Another animal survived a similar inoculation for five hours. The remaining animal survived an inoculation of 0.3 cc. Ten minutes later the rabbit was given an injection of 0.5 cc. One hour later, 1 cc. of lung extract was injected, and, although the animal's condition was critical, he survived. After three hours another inoculation of 1 cc. was given, followed immediately by convulsive seizures and death.

In all 4 animals the pathologic changes in the brain were essentially the same. In scattered areas there were sparse extravasations of red

blood cells into the subarachnoid space. An occasional perivascular space contained a small number of erythrocytes. Throughout the entire brain a large number of medium-sized and small vessels were partially to completely occluded with homogeneous eosinophilic material. In the case of the partially occluded vessels, this homogeneous material was observed only around the periphery of the lumen, leaving the central part of the lumen patent. Occasionaly fine threads of fibrin could be seen with the routine stain. With Mallory's phosphotungstic acid hematoxylin stain, however, an interlacing network of fibrin was frequently observed within the homogeneous intravascular clot (fig. 1). In none of these animals were there any prominent alterations of the

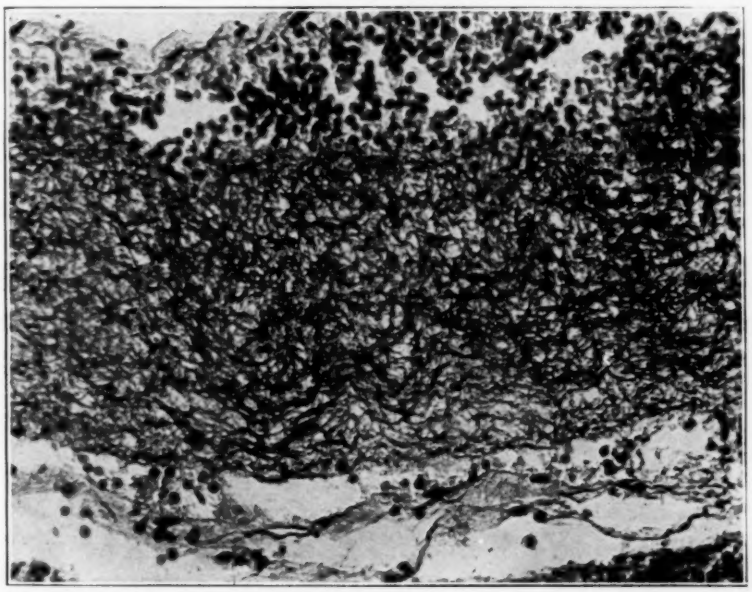

Fig. 1.—Thin-walled vessel filled with a dense interlacing network of fibrin. Mallory's phosphotungstic acid hematoxylin stain.

neurons. Usually a few scattered nerve cells showed slight chromatolysis. The myelin sheaths revealed no evidence of abnormality.

Subacute Experiments.—Four rabbits were included in this group. All the animals received from two to four intravenous inoculations of lung extract over a period of two to three days. Three of the animals received intravenous injections of heparin prior to inoculation of 1 cc. of lung extract. The dose of heparin varied from 6 to 100 units. Twenty-five to 100 units seemed to afford the animal complete protection. Smaller doses often seemed to prevent immediate convulsions and death; this protection was not complete, since the animal frequently became extremely ill. In 1 case opisthotonos developed. About three

minutes later convulsive seizures occurred and the animal died. Another animal survived inoculation with 1 cc. of lung extract on two consecutive days. A similar dose of lung extract produced immediate convulsive seizures and death on the third day.

The microscopic changes observed in the brain were identical in all animals and were very similar to those in the preceding group. Small extravasations of red blood cells were usually seen in the subarachnoid space and in a few scattered perivascular spaces within the parenchyma of the brain. The lumens of many of the cerebral vessels were partially to completely obstructed with homogeneous clots (fig. 2), in which Mallory's stain revealed numerous threads of fibrin, often arranged as a rather dense interlacing network. The nerve cells

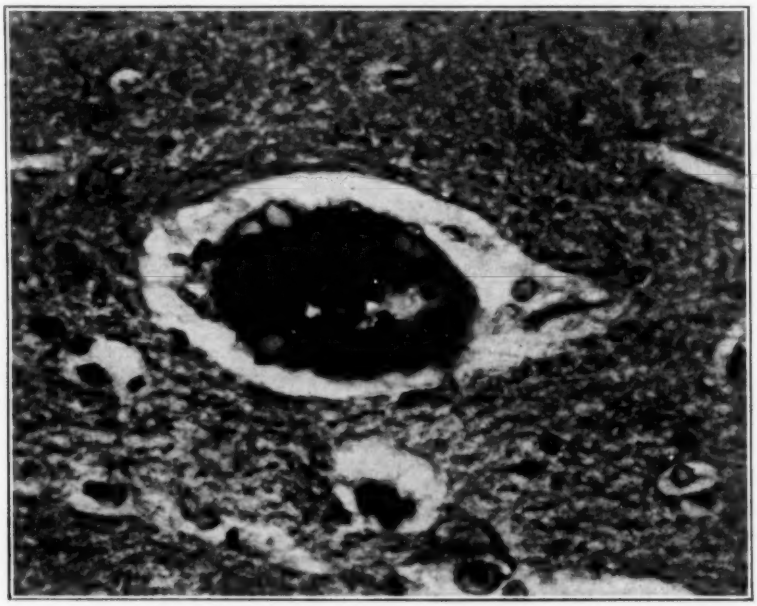

Fig. 2.—A small vessel partially occluded with a homogeneous clot. The central part of the lumen is still patent. Hematoxylin-eosin stain.

presented somewhat more prominent alterations. The cresyl violet stain revealed some chromatolysis. A rather large number of ganglion cells showed evidence of early shrinkage and pyknosis. The Weil stain demonstrated scattered areas of early perivascular degeneration of myelin. In a few places actual beginning fragmentation of the myelin sheaths was observed.

Subacute to Chronic Experiments.—Four rabbits comprised this group. The experiments extended over a period varying from six to twelve days. One animal received inoculations of 0.3, 0.5 and 0.75 cc. of lung extract intravenously at fifteen to thirty minute intervals. The

animal survived six days but later had convulsions and died after an inoculation of 0.3 cc. The other 3 rabbits received two injections of 1 cc. of the lung extract. Two died during convulsive seizures. The remaining animal exhibited paralysis of both hindlegs and urinary retention after the second intravenous injection. The animal was killed eight days later.

The pathologic changes observed in the brain were very similar to those in the preceding group. In all the brains, scattered vessels were partially to completely filled with homogeneous clots. Mallory's phosphotungstic acid hematoxylin stain revealed many of the clots to be composed largely of fibrin. In some vessels the strands of fibrin were very coarse and at times were fused into a solid mass. An occasional tiny perivascular extravasation of erythrocytes was observed. There were also disseminated areas of mild hemorrhage into the subarachnoid space. In 1 case the perivascular hemorrhages were most numerous in the cerebellum. Alterations of the nerve cells were relatively mild. Some neurons were pale, swollen and chromatolytic, while others were somewhat shrunken and hyperchromatic. Only mild alterations of the myelin sheaths had occurred, and those in widely separated areas of the brain.

Changes in the brain were relatively mild in the animal in which paralysis of the posterior limbs had developed. In this case the alterations in the spinal cord were more striking. Small perivascular hemorrhages were disseminated throughout the anterior horns of the cord. The anterior horn cells showed rather prominent alterations, similar to those occurring in the brain. Throughout the white matter of the cord much of the myelin was swollen and rarefied. In some areas there was actual beginning vacuolation of the myelin sheath. These alterations were best demonstrated by the Weil stain. In the vicinity of the central gray matter of the cord, an occasional capillary contained a clot similar to those observed in the brain.

Chronic Experiments.—There were 6 rabbits in this group. Three to thirteen intravenous injections of the lung extract were given over a period varying from two to eleven weeks. The sublethal inoculations ranged from 0.3 to 1 cc. of the extract. In only 1 case was heparin administered prior to the lung extract.

In 5 animals the pathologic changes in the brain were somewhat similar to those described in the preceding groups. In the 2 remaining animals somewhat different observations were observed. A case illustrative of each group will be described.

ANIMAL 3.—This rabbit received intravenous inoculations of 1 cc. of the homogenized saline extract at weekly intervals. The animal became slightly ill after the first two inoculations but survived. After the third injection convulsive seizures promptly appeared and resulted in death.

The external surface of the brain revealed rather prominent vascular congestion with scattered small areas of subarachnoid bleeding. Coronal sections of the brain demonstrated nothing of significance except for vascular congestion.

Microscopic study with the routine phloxine-hematoxylin stain revealed that scattered vessels throughout the brain contained homogeneous eosinophilic material. In many of the vessels this structureless material filled essentially the entire lumen (fig. 3). Occasionally fine threads of fibrin could be made out, suggesting that these intravascular structures were either clots or thrombi. With Mallory's phosphotungstic acid hematoxylin stain these lesions were frequently observed to consist of a dense intertwining network of fibrin. In longitudinal sections of the vessels long segments were seen to be filled with long threads of fibrin (fig. 4 *A*). The smaller vessels, including the capillaries, were most frequently involved. Relatively large vessels, however, were also occluded with the same homogeneous material, which with special stains was seen to contain a dense network of fibrin

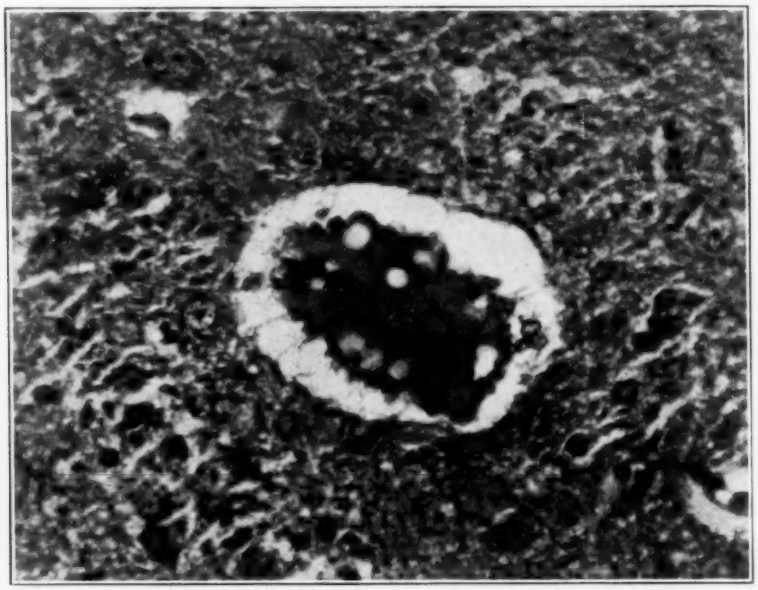

Fig. 3.—A small vein filled with homogeneous material resembling a clot. Only a few clumps of red cells are observed. Phloxine-hematoxylin stain.

(fig. 4 *B*). Some of the larger vessels in the choroid plexus were involved. Occasional vessels were filled with a pale yellow material, which contained little or no fibrin. The impression was that this structureless material consisted of serum adjacent to a contracted intravascular clot. Longitudinal sections of certain vessels demonstrated elongated clots, which had shrunk and contracted away from certain parts of the wall. There were a few scattered perivascular hemorrhages, together with slight extravasations of blood into the subarachnoid space.

The Nissl stain brought out alterations in a large percentage of the nerve cells throughout most of the brain. Throughout the cerebral cortex many neurons showed definite shrinkage and pyknosis, with some deformity of the cell body and its processes (fig. 5). Other cortical neurons showed prominent chromatolysis, which was often associated with paling of the cell nucleus (fig. 5). The cytoplasm of an occasional cell contained a few tiny vacuoles. A few ghost cells were seen in

scattered regions. There were occasional disseminated small foci of very early demyelination. These lesions were usually perivascular and were most numerous within the white matter of the cerebrum (fig. 6 *A*). In some regions degeneration of myelin was more diffuse. In the earliest stage of involvement the myelin

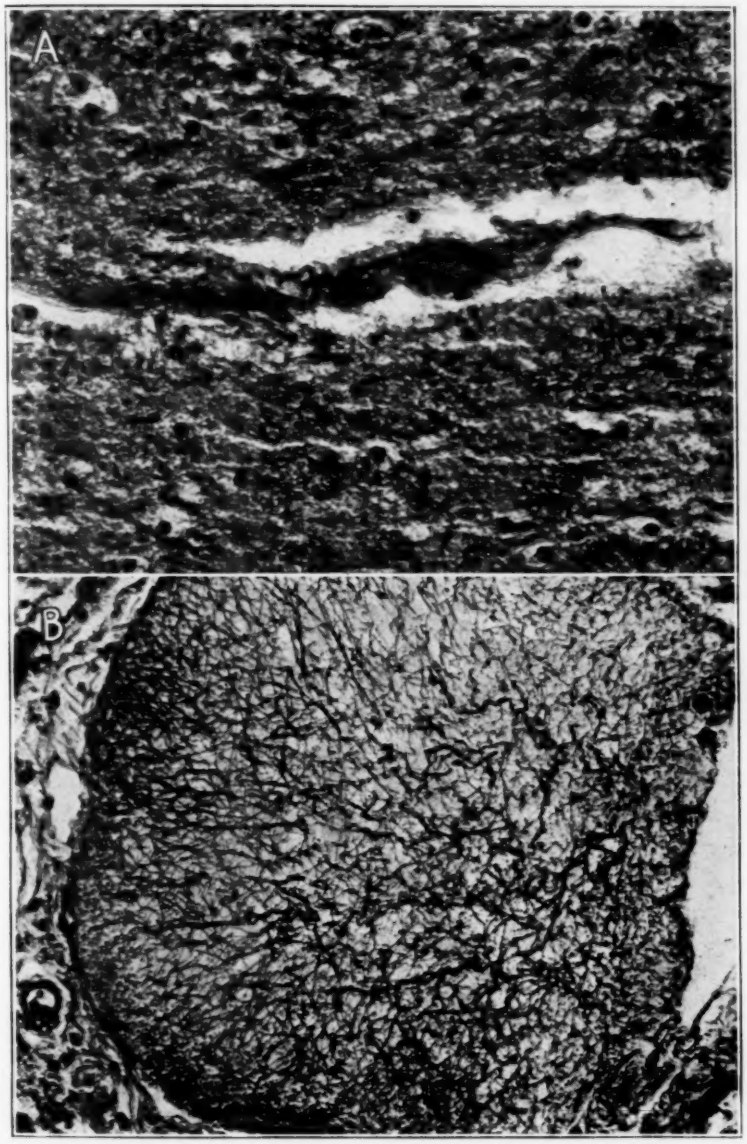

Fig. 4.—*A*, longitudinal section of a small cerebral vessel, showing long strands of fibrin filling the lumen of the vessel. *B*, lumen of a rather large vessel filled with a prominent network of fibrin. Mallory's phosphotungstic acid hematoxylin stain.

sheaths were merely slightly swollen and pale. In the more advanced lesion the Weil stain showed mild, but more definite, perivascular rarefaction of the myelin.

The neuropathologic alterations observed in this brain were similar to those noted in the brains of the other 4 rabbits of this group.

ANIMAL 29.—This rabbit became acutely ill after an intravenous injection of 1 cc. of the lung extract. The rabbit survived, however, without any apparent residual neurologic disturbance. The animal was then given injections of 0.3 cc. of the extract on five different occasions at intervals varying from five days to three weeks. The animal survived these inoculations, but six weeks later fatal convulsions followed another intravenous injection of 0.3 cc. of the extract.

Grossly, the brain showed prominent congestion and small subarachnoid extravasations of blood. Microscopic study demonstrated numerous intravascular clots similar to those previously described. There were also occasional small perivascular hemorrhages. Another type of involvement was frequently noted in the walls of vessels. This was evidenced by swelling and proliferation of the endothelial lining of the vessel, producing attenuation of the lumen. In scattered vessels polymorphonuclear leukocytes had infiltrated the walls of the vessels. Occasionally leukocytes invaded the perivascular spaces, resulting in small focal collections of neutrophils. In irregularly scattered regions a sparse invasion of the leptomeninges with polymorphonuclear leukocytes was observed. Throughout the brain alterations in the nerve cell were encountered similar to those already described except that they were much severer. There were also perivascular and diffuse areas of degeneration of myelin. The alterations in the myelin were also similar but were more prominent and severer.

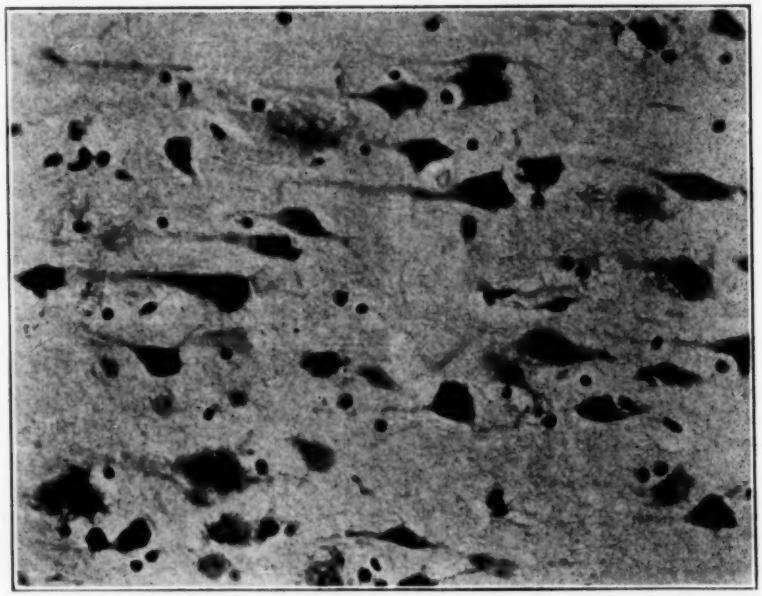

Fig. 5.—Cerebral cortex, showing shrinkage and pyknosis of many neurons. Others have become pale and lost most of their internal structure. Note the occasional ghost cell. Cresyl violet stain.

GUINEA PIGS

There were 5 animals in this group. All were given intracardiac injections of 1 cc. of a homologous lung extract. Two to three inocula-

tions were performed, at intervals of one day, in each case. Four of the animals died during the convulsive seizure that followed the final inoculation. The remaining animal survived the convulsive seizure but died the next day.

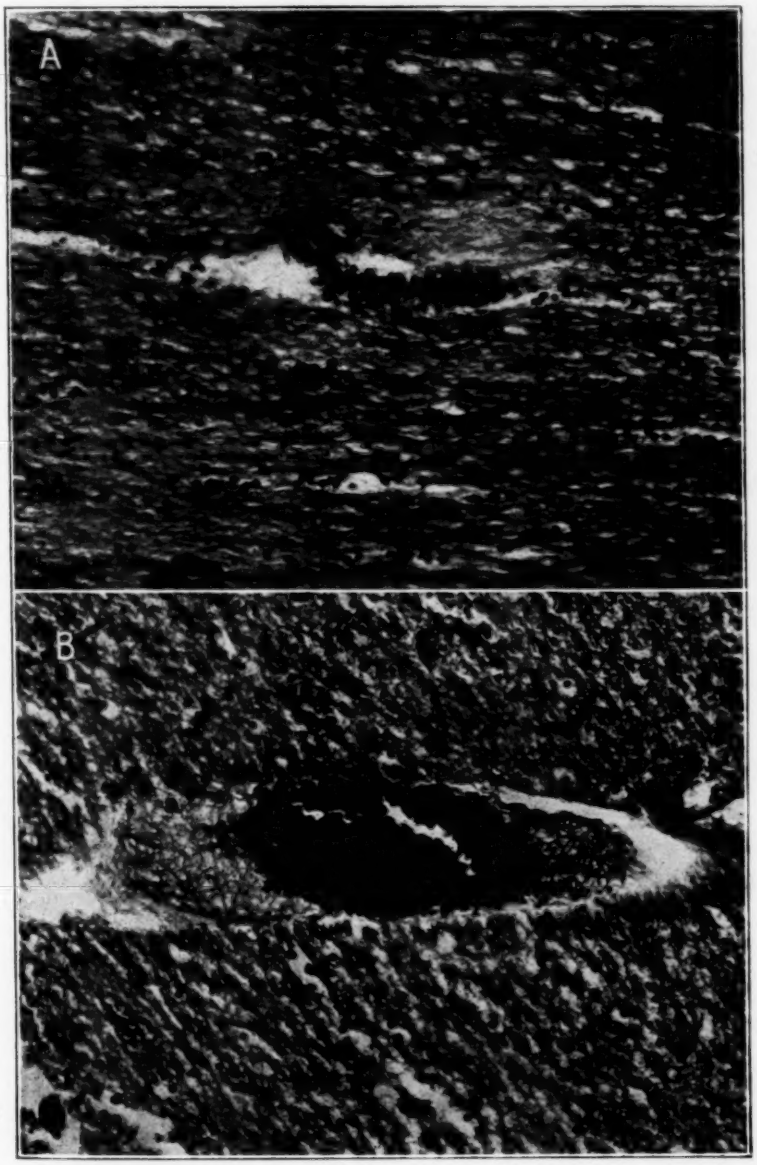

Fig. 6.—*A*, early perivascular demyelination, with partial loss of the tinctorial property of the myelin encircling the vessel; Weil's myelin sheath stain. *B*, peripheral zone of the lumen of the vessel occluded with a fibrin clot; Mallory's phosphotungstic acid hematoxylin stain.

In all 5 animals the brain showed a very similar type of pathologic alteration. Gross examination demonstrated moderate vascular con-

gestion. The microscopic observations were nearly the same as those described in the rabbits. Minute perivascular extravasations of blood were observed disseminated irregularly throughout the cerebral cortex. Numerous small vessels were partially to completely occluded with homogeneous clots, which with the Mallory phosphotungstic acid hematoxylin stain were seen to contain numerous threads of fibrin (fig. 6 *B*). In all animals there were rather prominent shrinkage and pyknosis of the neuron cells. The Weil stain revealed irregular areas in which the myelin was becoming pale. In 1 brain a sparse infiltration of polymorphonuclear leukocytes was observed around the adventitia of a few of the occluded vessels.

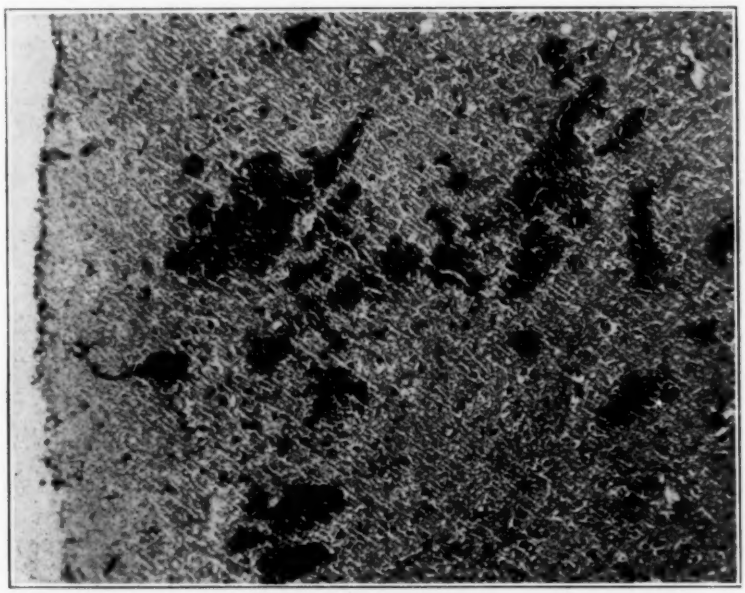

Fig. 7.—Prominent petechiae disseminated through the cortex; phloxine-hematoxylin stain.

DOGS

There were 7 dogs in this group.

One dog was given 20 cc. of homologous lung extract intravenously on two occasions, one week apart. After the first inoculation convulsive seizures developed. The animal survived but remained confused. At the time of the second inoculation the dog had not completely recovered. After the second injection another convulsive seizure developed. After remaining comatose for about one hour, the animal died.

Microscopic examination revealed petechial hemorrhages scattered throughout the brain. In certain areas of the cerebral cortex these petechiae were quite prominent (fig. 7). The hemorrhages generally consisted in an extravasation of the red blood cells into the perivascular spaces. Occasionally the bleeding actually extended into the surrounding cerebral parenchyma for a short distance. There

were no large hemorrhages. Throughout the entire brain the vessels were partially to completely filled with structureless material identical with that observed in the rabbits and the guinea pigs. These intravascular clots were somewhat more numerous in the gray matter but were also prominent in the white matter. The

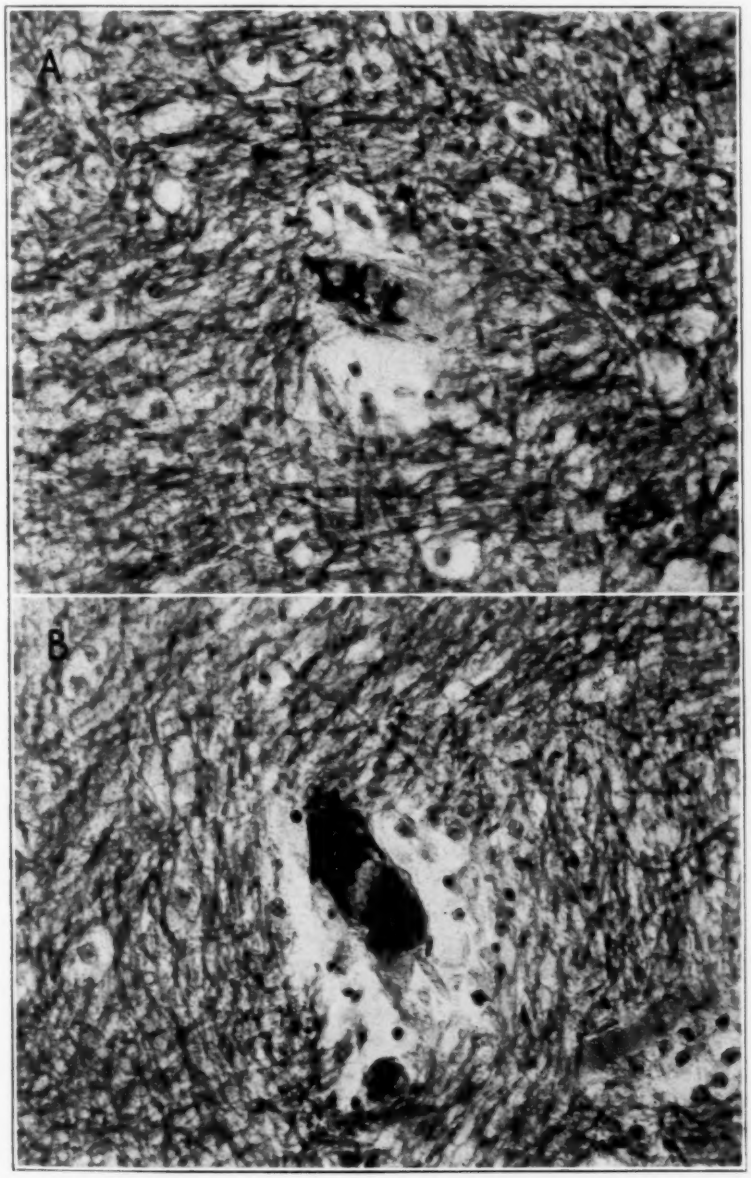

Fig. 8.—*A*, lumen of a tiny vessel containing very coarse strands of fibrin. *B*, coarse fibrin within the vessel fused into an almost solid mass. Mallory's phosphotungstic acid hematoxylin stain.

smaller vessels frequently contained irregular strands of fibrin (fig. 8 *A*). These were visible only with Mallory's phosphotungstic acid hematoxylin stain. In some

of the vessels the fibrin was very coarse and was frequently fused into a relatively solid mass (fig. 8 *B*). Throughout the brain there were prominent shrinkage and pyknosis of a large number of the ganglion cells. The myelin sheaths showed early irregular degeneration. This alteration in myelin tended to occur in regions where the intravascular clots were most numerous.

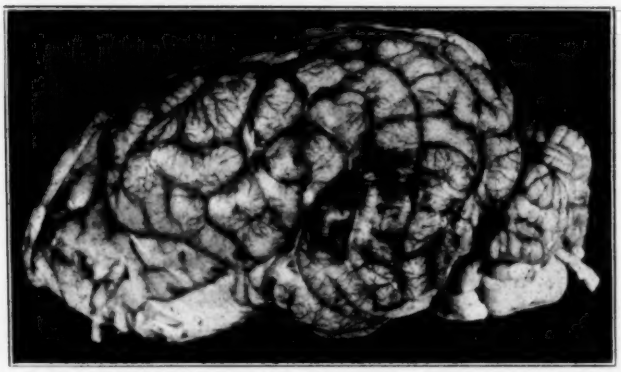

Fig. 9.—Vascular congestion and scattered punctate hemorrhages visible on the surface of the brain.

Fig. 10.—Lumen of a vessel filled with needles and threads of fibrin. Mallory's phosphotungstic acid hematoxylin stain.

In the remaining 6 dogs, the homologous lung extract was injected into the carotid artery. Inoculations, ranging from 2 to 5 cc., were given at intervals of one week. Three animals received three injec-

tions and the other 3 four injections. All the animals died in a convulsive seizure after the final inoculation, of 5 cc., of the extract.

The morphologic changes observed in the brain were similar in all the animals.

ANIMAL 52.—The brain of this dog will be described, since it revealed somewhat more striking hemorrhagic lesions than the others. Gross examination revealed a small amount of subarachnoid bleeding along some of the cerebral sulci. The entire surface of the brain was moderately congested. In a few areas there were small focal hemorrhages within the cerebral cortex. These could be seen on external inspection of the brain (fig. 9). Sparse subarachnoid hemorrhages, scattered perivascular hemorrhages and numerous intravascular clots were the outstanding microscopic observations. Mallory's phosphotungstic acid hematoxylin stain demonstrated interlacing threads of fibrin within the intravascular clots, even though they appeared structureless with the routine stain (fig. 10). Both the large and the small vessels were partially to completely occluded with these clots. Even with the Nissl stain, only mild alterations of the cerebral neurons were observed. With special staining, the myelin sheaths showed little evidence of degeneration.

In the other 5 dogs the hemorrhagic lesions in the brain were not so prominent; otherwise, the microscopic observations were essentially similar to those just described.

COMMENT

The striking observation in this series of experiments was the consistent and uniform pathologic alteration present in the brain. In all the animals numerous intravascular clots partially to completely occluded the lumens of many vessels. With the routine stain these clots appeared to be structureless and homogeneous, but with Mallory's phosphotungstic acid hematoxylin stain they were seen to contain numerous interlacing threads of fibrin. This fibrin was occasionally so coarse and dense that it was fused into almost solid masses. The earliest clotting occupied only the periphery of the vascular lumen, leaving the central part of the lumen patent. In occasional vessels structureless material, devoid of fibrin, filled the lumen. This seemed to represent serum adjacent to areas where the fibrin had contracted into a smaller mass.

In all the animals there were variable numbers of scattered petechial cerebral hemorrhages, as well as irregular areas of subarachnoid bleeding. The petechial hemorrhages tended to be more prominent in the dogs than in the rabbits or the guinea pigs. These hemorrhagic lesions were not so prominent or so consistent as the vascular clots. The latter seemed to be the more basic and fundamental manifestation of the pathologic process and probably gave rise to the vascular bleeding.

In 2 of the chronic rabbit preparations there were multiple perivascular inflammatory reactions, suggesting early abscess formation.

Intravascular clotting was prominent throughout both brains. There were rather advanced degenerative changes in the cerebral parenchyma secondary to the vascular occlusions, strongly suggesting that the vascular inflammation was a reaction to the destruction of tissue. Nevertheless, the suppurative nature of the inflammatory infiltrate makes it necessary for one to consider the possibility of the introduction of an infectious agent during the inoculations. Until further investigation is carried out, observations on these 2 rabbits cannot be adequately evaluated.

Except in these 2 rabbits, the cerebral parenchyma revealed only mild alterations. The neurons often showed swelling and chromatolysis. In the more chronic preparations they frequently also exhibited ischemic changes, such as shrinkage and pyknosis. The myelin sheaths of the nerve fibers were usually intact, with only mild alterations in occasional perivascular zones. In the longer experiments diffuse changes in the myelin were observed, in addition to the perivascular degeneration. There was no actual destruction of axons.

Comparison with the morphologic alterations observed in the human nervous system in cases of "pneumonic encephalitis" will show that the experimental lesions and those in the human brain are essentially identical. This suggests that both are the result of the same process, namely, the introduction of some product from the lung into the blood stream which facilitates blood clotting. These pathologic observations are additional proof that the cerebral complications of pneumonia may result from a disturbance of the clotting mechanism. This experimental reproduction of the lesions of so-called pneumonic encephalitis clearly indicates that pneumonitis liberates some product from the patient's lung which, in turn, produces an intravascular clotting in the cerebral vessels.

When one considers the frequency of infections of the respiratory tract and the possibility that a patient may be affected by a breakdown of his own lung tissue, it becomes apparent that this phenomenon may have implications of significance in other conditions—especially those in which clots or thrombi have been observed within the vessels of the nervous system. Such vascular lesions have been observed in association with a number of the encephalitides and with some of the degenerative maladies of the nervous system. Putnam and Alexander [16] recognized vascular thrombi within the brain in 3 cases of encephalitis after measles and in 2 cases of encephalitis after antirabies vaccination. Ferraro and Scheffer [17] noted venous thrombi associated with

16. Putnam, T. J., and Alexander, L.: Disseminated Encephalomyelitis: A Histologic Syndrome Associated with Thrombosis of Small Cerebral Vessels, Arch. Neurol. & Psychiat. **41**:1087 (June) 1939.

17. Ferraro, A., and Scheffer, I. H.: Encephalitis and Encephalomyelitis in Measles, Arch. Neurol. & Psychiat. **25**:748 (April) 1931.

encephalitis that followed measles. Scheinker [18] observed intravascular clots, which he regarded as part of his concept of "vasoparalysis and vasothrombosis," in 3 cases in which the etiologic factor was not clear. It is interesting to note that pneumonia was also present in 1 case.

In the numerous reports of postinfectious and secondary forms of encephalitis almost no mention is made of vascular clots or thrombi. It is possible that the small intravascular clots may have been overlooked or were not mentioned because they were regarded merely as a postmortem process, of no pathologic significance. This tendency to disregard these intravascular clots was experienced by us in our early cases of "pneumonia encephalitis," until we became aware of the consistency of their occurrence in a series of cases and observed that they were always present even when the hemorrhagic lesions were relatively inconspicuous. Putnam [19] noted thrombi in all his 3 cases of encephalomyelitis of undetermined cause.

For many years Putnam has been the chief exponent of the clotting theory of multiple sclerosis. He observed clots in the cerebral veins in 9 out of 17 cases of multiple sclerosis. Recently he has reduced the number of exacerbations in cases of disseminated sclerosis by giving "dicumarol" over a period (Putnam [20]). Because no changes were noted in the walls of the cerebral vessels, he postulated that the cause of the clotting or thrombosis must be in the circulating blood. Dawson,[21] who also observed thrombi in cases of multiple sclerosis, noted the normalcy of the walls of the involved vessels and the absence of the expected organization of the clots. We should like to point out that involvement and breakdown of the lung tissue has not been excluded in any of the aforementioned conditions. We suggest that this ability of the patient's own lung tissue to produce intracerebral clotting be given more consideration, since it may play a role in many neurologic diseases, and even in some of the obscure psychiatric conditions. An example of the latter are the behavior disorders following infections of the respiratory tract in which definite pneumonia is not present (Richter [22]).

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18. Scheinker, I. M.: Vasoparalysis and Vasothrombosis of the Brain in Infancy and in Early Childhood, Arch. Neurol. & Psychiat. **55**:216 (March) 1946.

19. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat. **37**:1298 (June) 1937.

20. Putnam, T. J.: The Use of Dicoumarin in the Treatment of Multiple Sclerosis, Tr. Am. Neurol. A., 1946, p. 26.

21. Dawson, J. W.: The Histology of Disseminated Sclerosis, Tr. Roy. Soc. Edinburgh **50**:517, 1916.

22. Richter, H. G.: Emotional Disturbances of Constant Pattern Following Nonspecific Respiratory Infections, J. Pediat. **23**:315, 1943.

Two interesting experiments should be mentioned in this discussion. The first, performed by Hoefer, Putnam and Gray,[23] was similar to ours in that these investigators were able to produce thrombi in the various organs, including the brain, of experimental animals by injecting lung and brain extracts. The type of reaction we obtained in our animals could not be produced with brain extract. From their report, one cannot determine whether they used homologous or heterologous extracts of the organs. In the second experiment, performed by Ferraro,[24] the results suggested to him an allergic basis for postinfectious encephalitides and degenerative neurologic conditions, such as multiple sclerosis. He made monkeys sensitive to either egg white or rabbit brain extract. These substances were then inoculated intracerebrally into the sensitized animals. Cerebral edema, petechiae, perivascular collections of microglial elements and leukocytes, parenchymal changes and thrombosis of small vessels resulted. It is difficult to apply the results of this experiment to human cases, since the brain extract was not from the same species of animal. Also, the antigen-antibody theory would not explain the immediate fatal convulsive seizures following the inoculations of homologous lung extract in an unsensitized animal.

In concluding this discussion, it is important to mention that the intravascular clots, produced by the breakdown of lung tissue in cases of pneumonitis or by the inoculation of homologous lung extract, differ from the usual thrombi. In the case of intravascular clotting the wall of the vessel, including the intima, is intact. The usual clumps and masses of platelets, so typical of thrombi, are not seen, except in the clots occluding the larger vessels. Instead of large numbers of platelets adhering to a roughened area of the intimal lining of the vessel, a dense network of fibrin forms within the lumen of the vessel to produce an intravascular clot. The process is similar to the experimental clotting produced by clotting agents within a test tube in the laboratory. We feel, therefore, that we are justified in concluding that the phenomenon is a true intravascular clotting which differs from thrombosis.

SUMMARY

The literature on the clinical and pathologic features of the cerebral complications of pneumonia is briefly reviewed.

Homologous lung extract was injected into 31 experimental animals. Most of the animals died in convulsive seizures after the last inoculation. Other organs or lung tissue from a heterologous species failed to produce a similar reaction.

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23. Hoefer, P. F.; Putnam, T. J., and Gray, M. G.: Experimental "Encephalitis" Produced by Intravenous Injections of Various Coagulants, Arch. Neurol. & Psychiat. **39**:799 (April) 1938.

24. Ferraro, A.: Pathology of Demyelinating Diseases as an Allergic Reaction of the Brain, Arch. Neurol. & Psychiat. **52**:443 (Dec.) 1944.

The brains of the experimental animals showed pathologic changes identical with those observed in cases of so-called pneumonic encephalitis in man. The fundamental lesion was a diffuse intravascular clotting. These clots differ from thrombi in that they consist of a homogeneous material in which special stains reveal a dense network of fibrin. The walls of the involved vessels are normal, and masses of platelets are rarely seen.

This study offers further proof that the encephalic complications of pneumonia are the result of an intravascular clotting. This clotting reaction is apparently set off by some product which is liberated from the lung during the pneumonitis.

The widespread frequency of infections of the respiratory tract and the possibility that a breakdown of the patient's tissue may produce intravascular clotting make it necessary to consider such a process in many conditions of unknown cause in which thrombi have been observed.

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BALLISM AND THE SUBTHALAMIC NUCLEUS (NUCLEUS HYPOTHALAMICUS; CORPUS LUYSI)

Review of the Literature and Study of Thirty Cases

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I. GENERAL CONSIDERATIONS

Historical Development of Hemiballism.—"Hemiballism" became associated with pathologic changes in the subthalamic nucleus (nucleus hypothalamicus; corpus Luysi) during the decade following 1920 (Jakob,[1] Martin,[2] von Sántha [3] and Matzdorff [4]).

That involuntary movements sometimes appeared after lesions localized in various parts of the brain had long been known. Weir Mitchell [5] and Charcot [6] recognized their frequent unilateral occurrence after apoplexies with the terms "posthemiplegic chorea" and "hemichorea." These terms, with the earlier contribution of "athetosis" by Hammond,[7] generally sufficed to distinguish the types of movements encountered.[8]

This study was aided by a grant from the William J. Matheson Commission.

From the Department of Neurology, Columbia University College of Physicians and Surgeons.

1. Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923, p. 328.

2. Martin, J. P.: Hemichorea Resulting from a Local Lesion of the Brain (Syndrome of the Body of Luys), Brain **50**:637-651, 1927.

3. von Sántha, K.: Zur Klinik und Anatomie des Hemiballismus, Arch. f. Psychiat. **84**:664-678, 1928.

4. Matzdorff, P.: Beiträge zur Pathologie des extrapyramidal-motorischen Systems; das Syndrom des Corpus Luysi, Ztschr. f. d. ges. Neurol. u. Psychiat. **109**:538-554, 1927.

5. Mitchell, S. W.: Post-Paralytic Chorea, Am. J. M. Sc. **68**:342-352, 1874.

6. Charcot, J. M.: Lectures on the Diseases of the Nervous System, translated by G. Sigerson, Philadelphia, Henry C. Lea, 1879, p. 214.

7. Hammond, W. A.: A Treatise on Diseases of the Nervous System, ed. 1, New York, D. Appleton and Company, 1871, p. 654.

8. Gowers (On Athetosis and Post-Hemiplegic Disorders of Movement, Med.-Chir. Tr., London **59**:271-325, 1876) disapproved of the terminology, not without foresight. In 1876 he wrote (page 277): "I have preferred not to use the term 'post-hemiplegic chorea' in speaking of any of these cases for two reasons: First, I think the term tends to confuse together several easily distinguishable varieties of movements, which may ultimately be found to depend upon pathological processes of different kinds or in different localities; secondly, the word chorea . . . were better not transferred to a symptom."

In the German literature, the flinging or throwing of the limbs arising from violent involvement of proximal musculature was described under the term "hemiballismus." Thus, Greidenberg [9] commented:

> The most frequent form of posthemiplegic motor disturbance, and hence the most adequately investigated, is without doubt hemichorea (posthemiplegic or postapoplectic hemichorea, *hemichorée posthemiplégique* [Charcot], hemikinesia [Hughlings Jackson], hemiballismus [Kussmaul]).

He described a case (without autopsy) in which this violent and flinging type of movement occurred unilaterally and referred to it as one of "typical hemichorea." Von Monakow [10] described the symptom as follows:

> Posthemiplegic chorea (hemiballismus of Kussmaul [11]) is characterized by a profusion of vigorous involuntary movements, sometimes rhythmic, at other times irregular, appearing in the hemiplegic limbs, especially in the arms and less frequently in the legs. The entire limb is affected . . . and (the movements) appear most often in the form of a flinging spasm (hemiballismus).

He noted that the symptom occurred with softenings and tumors, as well as with hemorrhages, and that it tended to appear when the lesion was in the posterior part of the thalamus or in the lenticulo-optic area.

With regard to the particular site of lesions evoking the symptom, Bonhoeffer [12] remarked, in his discussion on the *Bindarmtheorie*, that "the subthalamic region in the optic thalamus is observed to be involved in the majority of lesions in question." Touche,[13] describing unequivocal hemiballism in his case of "hemichorea," and observing that a hemorrhage completely masked the subthalamic nucleus, commented: "One might ask oneself whether the violence of the movements was not due specifically to the lesion of the body of Luys."[14]

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9. Greidenberg, B.: Ueber die posthemiplegischen Bewegungsstörungen, Arch. f. Psychiat. **17**:9-216, 1886.

10. von Monakow, C.: Gehirnpathologie, Vienna, A. Hölder, 1897, p. 318.

11. The suffix "—us" is a relic of little value from days when it was appended to many words, including "hypnotismus" and "somnambulismus"; and it may be conveniently dropped. References for Kussmaul's coining of "hemiballism" were not cited by Greidenberg, von Monakow or subsequent writers, e. g., H. Oppenheim (Lehrbuch der Nervenkrankheiten für Aerzte und Studierende, ed. 4, Berlin, S. Karger, 1905, p. 699), Jakob [1] and Herz.[21] As was found by Moersch and Kernohan,[24] search for the term in Kussmaul's published works is unrewarding. The word "ballism" comes through the Latin *ballista*, from the Greek βάλλειν, meaning "to throw."

12. Bonhoeffer, K.: Ein Beitrag zur Localisation der choreatischen Bewegungen, Monatschr. f. Psychiat. u. Neurol. **1**:6-41, 1897.

13. Touche: Deux cas d'hémichorée organique avec autopsie, Rev.neurol. **9**: 1080-1081, 1901.

14. The subthalamic nucleus (nucleus hypothalamicus), recognized by Luys (Recherches sur le système nerveux cérébro-spinal, Paris, J.-B. Baillière et fils, 1865, pp. 143-144) and described in detail by Forel (Untersuchungen über die Haubenregion und ihre oberen Verknüpfungen im Gehirn des Menschen und

(Footnote continued on next page)

Without using the term hemiballism, von Economo [15] described a case of posthemiplegic hemichorea of an especially violent nature, with a lesion in the contralateral subthalamic nucleus. Fischer,[16] calling the symptom "hemiballismus," described a similar lesion in case 5 of his series. It remained only for A. Jakob [1] to combine the picture in his case of "hemiballismus" (case 19, page 174) with the observations of von Economo and Fischer and establish the "syndrome of the corpus Luysi," which he described as follows:

> . . . The syndrome is a peculiar contralateral disturbance of movement which usually bears a similarity to choreiform movements of stormy nature, but surpasses by far the ordinary manifestations of chorea. It appears as irregular and incoordinated contorting movements of the muscle masses of an entire half of the body, with a pronounced tendency to attacks of twisting and turning. The symptom is called hemiballismus.

Authors since Jakob have emphasized the movements of the limbs more than those of the trunk. Jakob mentioned also that von Economo informed him orally that in the latter's case of 1910 [15] the condition, reported as "hemichorea," had been "wholly typical hemiballismus."

TABLE 1.—*Chronology of Thirty Reported Cases of Hemiballism Occurring with Localized Lesions of the Subthalamic Nucleus*

Decade.....	1880-1889	1890-1899	1900-1909	1910-1919	1920-1929	1930-1939	1940-1947
No. of cases...	2	0	1	3	8	14	2

By 1930 the frequent appearance of hemiballism contralateral to a lesion of the subthalamic nucleus had become fairly well established (table 1).

Relation of Ballism to Chorea.—Whether the symptom of hemiballism can be distinguished from other patterns of involuntary movement has been the subject of much controversy. Wilson [17] did not

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einiger Säugetiere, mit Beiträgen zu den Methoden der Gehirnuntersuchung, Arch. f. Psychiat. **7**:393-495, 1877), is roughly a lens-shaped structure situated on the fibers of the internal capsule as they pass ventrocaudad at the level of the mamillary bodies. What is known concerning its anatomy and connections was summarized by Sano (Beitrag zur vergleichenden Anatomie der Substantia nigra, des Corpus Luysii und der Zona incerta, Monatschr. f. Psychiat. u. Neurol. **27**: 110-127, 1910 [subthalamic nucleus, pp. 114-117]) and Ariëns Kappers, Huber and Crosby (The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936, vol. 2, pp. 1174-1175).

15. von Economo, C. J.: Beitrag zur Kasuistik und zur Erklärung der posthemiplegischen Chorea, Wien. klin. Wchnschr. **23**:429-431, 1910.

16. Fischer, O.: Zur Frage der anatomischen Grundlage der Athetose double und der posthemiplegischen Bewegungsstörung überhaupt, Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:463-486, 1911.

17. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940.

use the term hemiballism and stated only that "vascular and other lesions in various cerebello-mesencephalo-strio-thalamo-cortical fields can induce chronic choreas." Jelliffe and White [18] did not mention the subject, but the majority of authors of textbooks describe the symptom briefly and ascribe it to lesions of the contralateral subthalamic nucleus. The *Quarterly Cumulative Index Medicus* lists cases of hemiballism under headings of "chorea," "athetosis" and "spasm."

Martin [19] denied that a differentiation of hemiballism from other choreas was justified except on the basis of quantitative aspects of the movements. Wenderowic,[20] arguing "non sunt multiplicanda entia sine necessitate," affirmed the existence of a quantitative difference, susceptible only to "intuitive" analysis. Herz,[21] after motion picture studies of a variety of involuntary movements, including 2 cases of ballism (without autopsy), suggested that the mechanisms of chorea were not completely identical with those of ballism.

Van Sántha [3] and Balthasar [22] spoke for a clear differentiation of hemiballism from other choreas on the basis of form or pattern of the movements, and Davison and Goodhart,[23] expressing agreement with these authors, asserted that the pattern depended on which structure was involved and that ballism appeared only when the subthalamic nucleus was destroyed. Moersch and Kernohan [24] noted that the terms hemichorea and hemiballism were used interchangeably, but reserved hemiballism for the hemichorea of elderly patients, making their distinction not on the pattern of the movements but on the incidence, onset, course and similar features. Bucy [25] stated that "the definition of hemiballismus rests primarily upon the pathology and not upon the clinical features." Keschner [26] protested that "although

18. Jelliffe, S. E., and White, W. W.: Diseases of the Nervous System, ed. 6, Philadelphia, Lea & Febiger, 1935.

19. (*a*) Martin.[2] (*b*) Martin, J. P., and Alcock, N. S.: Hemichorea Associated with Lesions of the Corpus Luysi, Brain **57**:504-516, 1934.

20. Wenderowic, E.: Ueber das anatomische Substrat des Hemiballismus bzw. der Hemichorea, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:78-112, 1928.

21. Herz, E.: Die amyostatischen Unruheerscheinungen: Klinisch-kinematographische Analyse ihrer Kennzeichen und Begleiterscheinungen, J. f. Psychol. u. Neurol. **43**:3-182, 1931.

22. Balthasar, K.: Ueber das Syndrom des Corpus Luys an Hand eines anatomisch untersuchten Falles von Hemiballismus, Ztschr. f. d. ges. Neurol. u. Psychiat. **128**:702-720, 1930.

23. Davison, C., and Goodhart, S. P.: Monochorea and Somatotopic Localization, Arch. Neurol. & Psychiat. **43**:792-803 (April) 1940.

24. Moersch, F. P., and Kernohan, J. W.: Hemiballismus: A Clinicopathologic Study, Arch. Neurol. & Psychiat. **41**:365-372 (Feb.) 1939.

25. Bucy, P. C.: The Neural Mechanisms of Athetosis and Tremor, J. Neuropath. & Exper. Neurol. **1**:224-239, 1942.

26. Keschner, M.: Dyskinesias, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 10, p. 307.

the pattern of ballistic movement has not the slightest resemblance to that of choreiform movements, yet many physicians designate these cases as hemichorea." In recent years a converse tendency has become apparent (noted also by Bertrand and Christophe,[27]) by which a variety of hemilateral involuntary movements are reported as "hemiballism," without support of a full description of symptoms or of autopsy.

An indication of the semantic character of the problem arose during a meeting of German neurologists, at which Hallervorden [28] presented a motion picture record of a case of "lively hyperkinesia," with a diagnosis of hemiballism, but "the anticipated hemorrhage into the corpus Luysi did not appear" and only senile changes of the striatum, thalamus and subthalamic nuclei were to be seen. In the ensuing discussion, Bonhoeffer would not agree that the movements described were those of ballism and stated that he preferred to designate them as those of senile chorea only.

Thus, it appears that there has been a general, but not unanimous, acknowledgment that a violent hemichorea, appropriately termed hemi-

TABLE 2.—*Terminology Employed for Clinical Phenomena Accompanying Localized Lesions of Subthalamic Nucleus*

Term used			Ballism	Chorea	Other Terms
No. of cases			20	8	2
Language of report	German	English	French	Italian	Spanish
No. of cases	16	6	5	2	1

ballism, succeeds lesions localized in the contralateral subthalamic nucleus. There is disagreement whether the symptom is specific for, and limited to, such lesions. To determine whether hemiballism as a symptom is an entity and to ascertain what relation, if any, the subthalamic nucleus bears to the symptom was the purpose of this review of the clinical and clinicopathologic literature.

Method of Study.—Ballism was considered a pattern of dyskinesia characterized by continuous, violent, coordinated involuntary activity involving the axial and proximal appendicular musculature such that the limbs were flung about. Search was made in the literature for mention of this symptom, regardless of terminology (table 2), and for the pathologic changes with which it was associated. Descriptions of pathologic changes in the subthalamic nuclei were also sought, whether or not they were accompanied with symptoms and signs.

27. Bertrand, I., and Christophe, J.: Étude anatomo-clinique d'un cas d'hémiballisme: Hémorrhagie linéaire du corps de Luys avec extension au locus niger, Rev. neurol. **74**:140-141, 1942.

28. Hallervorden: Pathologisch-anatomische Demonstrationen; Hemiballismus, Zentralbl. f. d. ges. Neurol. u. Psychiat. **73**:724, 1934.

From these two approaches a series of approximately 60 case reports was obtained. Reports in which descriptions of movements and pathologic changes were considered sufficiently complete and accurate were analyzed. Thirty of these cases (part II) proved to be instances of hemiballism associated with pathologic changes localized in the subthalamic nucleus. The circumstances present in the 30 remaining cases are discussed in a separate section (part III), which includes reports of 10 cases of hemiballism and lesions of the subthalamic nucleus without sufficient clinical or pathologic description to merit inclusion in part II.

II. HEMIBALLISM WITH LOCALIZED LESIONS OF SUBTHALAMIC NUCLEUS

Clinical Manifestations.—The clinical pictures in the 30 cases collected by the method outlined in the preceding section were so similar that they may be presented in composite form.

The average age of the patients was 64, with an age distribution unusual for its approximation to the "normal," or bell-shaped, curve (table 3). Seventeen patients were females and 13 males. The clinical finding of arteriosclerosis and hypertension was common, and the latter was frequently present to a formidable degree, but rather good health prior to onset of the symptom was notable.

TABLE 3.—*Age Distribution of Patients with Hemiballism and Localized Lesions of the Subthalamic Nucleus*

Age group, yr	40-49	50-59	60-69	70-79	80-89	Not Stated
No. of cases	1	8	10	8	2	1

As a rule the onset and development of the symptom were sudden (over a period of hours) and could be correlated largely with the nature of the pathologic change (table 8); but in Wulff's case,[29] with a slow-growing tubercle in the subthalamic nucleus, the movements also appeared suddenly.

The involuntary activity that soon reached such dramatic expression began at times with little more than twitchings at the angle of the mouth or with the flinging of an article from the hand. Although in many of the cases of hemorrhage the movement was imposed on a previously hemiplegic side (always coincident with return of a degree of voluntary control), transient aphasia or a period of malaise was frequently the only preliminary indication of the violent symptom later to appear.

The involuntary movements were usually confined to the side opposite the lesion (hemiballism), although less typical ballistic movements

29. Wulff, H.: Corpus Luysi und das hemiballistische Syndrom, Acta psychiat. et neurol. **7**:999-1019, 1932.

were observed ipsilaterally in some instances. Monoballism was described by Marcus and Sjögren,[30] and, by strict definition, the cases of Greiff[31] and Balthasar[22] (first case) showed monoballism of an upper extremity, rather than hemiballism. The head was sometimes jerked about on the neck. Speech and swallowing were now and then impaired, and at times even extrusion of the tongue was forceful and continuous. The face participated by violent grimacing in several cases, and the relation of its involvement to the topographic distribution of destruction within the nucleus suggested to some authors a degree of somatotopy (see page 685).

Such movements are not uncommon with many of the choreas, however, and it was in the extremities that the most remarkable and distinctive movements appeared. Flingings and hurlings of the upper extremities and kickings and poundings of the lower extremities, of the greatest abruptness and violence, persisted through every waking moment. Their force and amplitude derived from the coordinating activity of the muscles about the proximal joints and of the related axial musculature. The muscles of the trunk would sometimes contribute further to the pattern by twisting the torso and hips. Hypotonia of the affected muscles, noted as present in 9 cases, and present by inference from the description in 4 other cases, appeared to contribute to the amplitude and freedom of the activity. Abrasions and lacerations from the flailings were commonly reported complications.

Although movements might repeat themselves, no regular rhythm was followed. Sometimes appearing almost "voluntary" in their coordination, the patterns of flexion and extension, abduction, adduction and rotation changed constantly without particular sequence, and could be interrupted by the patient only momentarily, if at all, and with great effort. They appeared almost instantly on waking, usually grew worse during the day, were uniformly and almost characteristically exacerbated by attention or emotion, tended to appear in increased violence after external restraint and were constantly present except during sleep, when they ceased altogether, as in any form of chorea.

Chloral hydrate, paraldehyde, scopolamine, morphine, stramonium, curare and atropine were given therapeutic trial in various cases. The sedatives decreased the violence of the movements and sometimes permitted sleep, which might otherwise have been unobtainable. Although autopsy was not performed in their cases, Schob[32] described

30. Marcus, H., and Sjögren, H.: L'hémiballisme et le corps de Luys, Rev. neurol. **70**:1-28, 1938.

31. Greiff, F.: Zur Localization der Hemichorea, Arch. f. Psychiat. **14**:598-624, 1883.

32. Schob, F.: Hemichorea und Hemiathetose nach Schädeltrauma, Deutsche Ztschr. f. Nervenh. **65**:210-218, 1920.

an instance of hemiballism following fracture of the skull which was relieved by subsequent excision of a cyst, and Jermutowicz [33] and Kulenkampff [34] reported surgical efforts to ameliorate the symptom.

Patients seized with such extensive involuntary activity were distraught and exhausted; they attempted to quiet their afflicted extremities with their normal ones, lay on them or restricted them with bedclothes. Bertrand and Garcin [35] reported a case in which lashing of the arm to the body was resorted to by the patient's husband. In Marcus and Sjögren's [30] second case the patient committed suicide by drowning on discharge from the hospital, almost two years after onset of the movements.

Symptoms of confusion, disorientation or dementia, which some authors (e. g., Martin [19] and Bertrand and Christophe [27]) sought to include in the syndrome of damage to the nucleus, were by no means

TABLE 4.—*Incidence of Mental Symptoms with Lesions of the Subthalamic Nucleus*

A. Cases of hemiballism with lesions of nucleus and lesions elsewhere (30)		
Mental symptoms noted to be absent		6
Mental symptoms present		14
Of these, present only terminally	3	
Mental symptoms not noted		10
Total		30
B. Cases in section A with localized lesions of nucleus only (13)		
Mental symptoms noted to be absent		4
Mental symptoms present		6
Of these, present only terminally	2	
Mental symptoms not noted		3
Total		13

invariably associated with such a pathologic change (table 4). Only 4 of the 13 patients with localized lesions alone showed mental symptoms other than those which appeared during the terminal stage of the illness. Sensory or reflex changes were absent unless there were lesions elsewhere in the brain.

Death occurred within several days to several months of the onset. Hemiballism persisted unabated until death, for as long as twelve (Touche [13]), or even nineteen (von Sántha [3]), months. Although in

33. Jermutowicz, W.: Un cas d'hémiballismus partiellement amélioré après intervention périphérique, Rev. neurol. **55**:374-375, 1931.

34. Kulenkampff, D.: Ueber die sogenannte Hemichorea posthemiplegica (Hemiballismus) und die Bedeutung der Pyramidenbahnen, Zentralbl. f. Chir. **65**:2466-2470, 1938.

35. Bertrand, I., and Garcin, R.: Étude anatomo-clinique d'un cas d'hémiballismus: Lésion dégénérative du corps de Luys et de la zona incerta, Rev. neurol. **2**: 820-828, 1933.

at least 2 cases (Marcus and Sjögren,[30] cases 4 and 5 [without autopsy]) the condition showed remission, the prognosis for recovery was grave. Patients rarely lived with the symptom more than four or five weeks; and the commonest cause of death was pneumonia (table 5). During the terminal coma the movements frequently diminished, or ceased entirely.

Pathologic Changes in the Subthalamic Nucleus.—Destruction of the subthalamic nucleus, without noteworthy coexisting or antecedent pathologic change elsewhere, was described in 13 of these 30 cases of hemiballism.

Owing to the numerous and intimate relations of the nucleus, one or more of the adjacent structures were not uncommonly involved. These structures included the overlying dorsal divisions of the ansa lenticularis and thalamic fasciculi; the zona incerta, lying between them; the internal capsule, lateral to the nucleus; the substantia nigra, ventrally, and the fusion of the dorsal and ventral divisions of the ansa lenticularis, medially (table 6). But in all these cases the lesion

TABLE 5.—*Causes of Death in Cases of Hemiballism*

Cause of death	Pneumonia	Cardiac Failure	"Exhaustion"	Cerebrovascular Disease	Pyelitis	Suicide	No Information	Total
No. of cases	13	3	3	1	1	1	8	30

of the nucleus was common, and in the cases of Fischer[16] and Pelnář and Sikl[36] it was limited strictly to the nucleus, a remarkable confinement in a structure roughly the shape and dimensions of a small lima bean.

Destruction localized to the subthalamic nucleus, but having coexisting or antecedent pathologic changes elsewhere, occurred in 17 of the 30 cases (table 7). In addition to hemiballism, symptoms referable to other regions of the brain were present; but in none of the cases was the significance of the localized damage to the nucleus really in question. In evaluation of the pathologic changes, the estimated pathologic age of the lesion in relation to the duration of the hemiballism was frequently helpful, since the observation of an old softening in the cerebellum and a recent hemorrhage in the subthalamic nucleus left little doubt as to which was related to a symptom of eight days' duration. The presence of gross cerebral arteriosclerosis, reported in the majority of cases, might have been anticipated from the advanced age of the patient group.

36. Pelnář, J., and Sikl, H.: L'hémiballisme, le ballisme aigu et le corps de Luys, Rev. neurol. **2**:328-331, 1929.

Despite the sequence of published cases and the increasing concentration of attention on the region, no case appeared in which an asymptomatic localized lesion of the nucleus was present.

As was pointed out by Martin,[2] it is possible that certain structures must remain intact for hemiballism to appear on destruction of the nucleus. In Kelman's [37] first case the movements ceased during hospitalization, with a dramatic worsening of the patient's status; and autopsy revealed that practically the entire hemicerebrum contralateral to the ballistic movements had been destroyed by a hemorrhage which

TABLE 6.—*Localized Pathologic Change in the Subthalamic Nucleus Without Lesions in Distant Parts of the Cerebrum*

Lesion	Author	Date	Adjacent Area Affected
Hemorrhage	von Economo [15]	1910	Substantia nigra, tegmentum, thalamus
Hemorrhage	Fischer [16]	1911	None
Hemorrhage	Campora [43]	1922	Substantia nigra, capsule of red nucleus, Forel's field
Hemorrhage	Martin [2]	1927	Internal capsule, lenticular fasciculus (H_2)
Hemorrhage	Jakob, C.: Arch. argent. de Neurol. **2**: 1-15, 1928	1928	Substantia nigra, rubrolenticular fasciculus, zona incerta
Hemorrhage	Pelnář and Sikl [36]	1929	None
Hemorrhage	Martin [19b]	1934	Lenticular fasciculus, zona incerta
Précriblé	Bertrand and Garcin [35]	1933	Capsule of red nucleus, zona incerta
Précriblé	Drouet, P, L., Michon, P., and others: Bull. et mém. Soc. méd. d. hôp. de Paris **54**: 1085-1089, 1938	1938	Zona incerta
Hemorrhagic softening	Canfield, R. M., and Putnam, J. J.: Bost. M. & S. J. **111**: 220-223, 1884	1884	Internal capsule, substantia nigra, tegmentum
Metastatic carcinoma	Bonhoeffer, K.: Monatschr. f. Psychiat. u. Neurol. **77**: 127-143, 1930	1930	Substantia nigra, thalamic fasciculus (H_1)
Tubercle.....	Wulff [29]	1932	Internal capsule, rubrothalamic fasciculus, lenticular fasciculus
Infarcts	Moersch and Kernohan [24]	1939	Lenticular and thalamic fasciculi?

was distinct from a hemorrhage into the subthalamic nucleus of the same side, and apparently had occurred subsequent to it. Again, in Segall's case [38] of hemorrhage into the subthalamic region, extensive involvement of the midbrain, including almost the whole internal capsule, and ventricular hemorrhage were present, and hemiballism failed to appear. Balthasar [22] commented on a case of hemorrhage involving the subthalamic nucleus, without involuntary movements, in which the

37. Kelman, H.: Hemiballismus: Clinicopathologic Study of Two Cases, J. Nerv. & Ment. Dis. **101**:363-371, 1945.

38. Segall, E.: Ein Beitrag zur Pathologie des Corpus Luysi, Monatschr. f. Psychiat. u. Neurol. **52**:156-161, 1922.

TABLE 7.—*Localized Lesions of the Subthalamic Nucleus Complicated by Lesions Elsewhere, and Associated Ballism*

Case	Date	Adjacent Areas Affected	Site of Other Lesions
Hemorrhage into Subthalamic Nucleus			
Greiff [31]	1883	Internal capsule	Ipsilateral thalamus and occipital lobe; contralateral cerebellar hemisphere
Juba and Rakonitz [48]	1937	Lenticular fasciculus	Ipsilateral pallidum and anterior nucleus of thalamus; contralateral substantia nigra
Kelman [37] (first case)	1945	None ?	Hemisphere, thalamus and basal ganglia (subsequent to subthalamic lesion)
Matzdorff [4]	1927	Thalamic and lenticular fasciculi; ansa lenticularis	Ipsilateral striatum and thalamus
von Sántha [3]	1928	Zone incerta; lenticular fasciculus	Contralateral cortex; basal ganglia and thalamus
Uiberall, H., and Samet-Ambrus, V.: Ztschr. f. d. ges. Neurol. u. Psychiat. **131**: 502-513, 1913	1913	Substantia nigra; thalamic fasciculus	Ipsilateral pallidum and putamen
Wenderowic [20]	1928	Internal capsule; lenticular fasciculus	Ipsilateral occipital lobe
von Sántha [47]	1932	Lenticular fasciculus	Contralateral lateral thalamus and medial geniculate body
A. Jakob [1] (case 19)	1923	Rubrothalamic fasciculus; thalamic and lenticular fasciculi	Bilateral status cribrosus of striopallidum
Touche [13]	1901	Internal capsule; red nucleus; substantia nigra	Ipsilateral lateral nucleus of thalamus; retrolenticular internal capsule
Marcus and Sjögren [30] (case 1)	1938	Region of subthalamic nucleus	Pons
Gregory, H. S.: New York State J. Med. **38**: 635-636, 1938	1938	Tegmentum	Basal ganglia (scattered softenings)
Syphilitic Necrosis of Subthalamic Nucleus			
Bodechtel, G., and Hikl, W.: Arch. f. Psychiat. **102**: 654-669, 1934	1934	Red nucleus (anterior part)	Contralateral pallidum; ipsilateral juxtathalamic area; ansa lenticularis and lenticular fasciculus (H_2)
Kutch, T.: Ztschr. f. d. ges. Neurol. u. Psychiat. **164**: 404-416, 1939	1939	Internal capsule; lenticular fasciculus	Meninges; contralateral caudate nucleus; putamen and internal capsule
Softenings of Subthalamic Nucleus			
Balthasar [22]	1930	None ?	Contralateral cortex; striopallidum and thalamus
Marcus and Sjögren [30] (case 2)	1938	Internal capsule	Ipsilateral thalamus
Neoplasm Metastatic to Subthalamic Nucleus			
Bremme [42]	1919	Internal capsule; substantia nigra; lenticular fasciculus	Contralateral cerebellum and cerebellar peduncle

dorsal thalamus, the striatum and much medullary substance were also destroyed. It is of interest that the movements of hemiballism in Touche's case [13] ceased temporarily during two intercurrent attacks of bronchopneumonia.

Symptoms Referable to the Autonomic Nervous System.—Few writings on hemiballism have failed to include comment on the association of symptoms of disturbance of the autonomic nervous system with lesions of the subthalamic nucleus. An autonomic function was suggested by the experiments of Karplus and Kreidl,[39] whose stimulation of the region in animals produced a galaxy of symptoms referable to activity of the sympathetic nervous system. Speculations by Schrottenbach [40] and Gerstmann [41] on their clinical experience served to fortify the concept. Of the 30 cases which form the basis of this review, symptoms of autonomic disturbance which might be related to the pathologic changes in the subthalamus were present in only 5.

TABLE 8.—*Type of Lesion and Mode of Onset*

No. of Cases	Type of Lesion	Mode of Onset *	
		Sudden	Gradual
19	Hemorrhage	15	1
3	Softening	2	1
2	Metastasis	0	2
2	Syphilitic necrosis	0	2
1	Tubercle	1	0
1	Infarct	1	0
2	Degeneration	1	1
30		20	7

* Information lacking in 3 cases.

In Bremme's [42] case there were hyperhidrosis over the left side, especially of the face, and vasodilatation on the same side of the face. A metastatic lesion involved the subthalamic nucleus, internal capsule, substantia nigra and lenticular fasciculus on the left side, and the ballistic movements were contralateral. In Martin's case,[2] moderate hemihyperhidrosis was present on the side of the ballistic movements, and a hemorrhage involved the contralateral subthalamic nucleus, inter-

39. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: I. Zwischenhirnbasis und Halssympathicus, Arch. f. d. ges. Physiol. **129**:138-144, 1909.

40. Schrottenbach, H.: Beiträge zur Kenntnis der Uebertragung vasovegetiver Funktionen im Zwischenhirn, Ztschr. f.d.ges.Neurol. u. Psychiat. **23**:431-510, 1914.

41. Gerstmann, J.: Zur Frage der sympathischen Gehirnbahnen, Jahrb. f. Psychiat. u. Neurol. **34**:287-321, 1913.

42. Bremme, H.: Ein Beitrag zur Bindarmchorea, Monatschr. f. Psychiat. u. Neurol. **45**:107-120, 1919.

nal capsule and lenticular fasciculus. In Greiff's [31] case there were hyperthermia and vasodilatation of the arm on the side of the ballistic movements and a hemorrhage involving the contralateral subthalamic nucleus and internal capsule; hemorrhages also existed in the occipital lobe on the side of the lesion and in the medullary core of the cerebellar hemisphere on the side of the symptom. Pallidohypothalamic fibers known to run in the ansa lenticularis were interrupted in the first 2 cases and may have been implicated in the third. Why the autonomic symptoms were ipsilateral to the lesion in Bremme's case and contralateral in the other 2 cases is not clear. Somnolence, possibly a symptom of "vegetative function," was present in the cases of Matzdorff [4] and Wenderowic,[20] but its significance in patients 80 and 81 years of age, respectively, is questionable. Edema of the affected hand and forearm was noted clinically in Bertrand and Garcin's [35] case and at autopsy in Campora's [43] case, being associated in the latter with lividity

TABLE 9.—*Somatotopical Relations of the Subthalamic Nucleus in Cases of Hemiballism*

	No. of Cases
Favoring somatotopic relations	
Face affected and oral pole destroyed	17
Face free and oral pole intact	2
Not favoring somatotopic relations	
Face involved and oral pole intact	1
Face free and oral pole involved	1
Information lacking	9
Total	30

of the affected side. Reference may be made to Friedman's [44] reports of hemiedema associated with hemiplegia, but whether these signs were secondary to an autonomic change or whether they were due to the abnormal muscular activity of hemiballism is difficult to decide.

In the remaining 25 cases no mention was made of symptoms of autonomic disturbance. The equivocal nature of the 5 cases noted here renders it doubtful whether the subthalamic nucleus possesses any autonomic function.[45]

43. Campora, G.: Sopra un caso di emicorea con reperto necroscopio, Pathologica **14**:41-43, 1922.

44. Friedman, A. P.: Hemiedema in Hemiplegia: Report of Three Cases, Bull. Los Angeles Neurol. Soc. **7**:194-197, 1942.

45. It may be reiterated (Wilson [58]) that deduction of the function of a neural structure from the symptoms following its destruction is not always warranted, an objection which applies to analysis of kinetic, as well as autonomic, activities of the subthalamic nucleus by this method.

Somatotopic Relations.—The Vogts [46] (page 774) expressed the belief that a definite topical relation exists between the parts of the striopallidum and the subthalamic nucleus. Von Sántha [47] concluded that the head, arms, trunk and legs were represented by different parts of the nucleus, proceeding in an orocaudal direction, because the face was affected and the entire nucleus destroyed in his first case,[3] while no involuntary facial movements appeared in his second case,[47] in which the oral pole was spared. Martin [19b] and Juba and Rakonitz [48] submitted their cases of hemiballism as evidence of a somatotopic arrangement in the subthalamic nucleus. Table 9 suggests, in agreement with these authors, that involuntary facial movements usually occur with involvement of the oral pole of the structure.

TABLE 10.—*Association of Involuntary Movement with Nonfocal Lesions in the Subthalamic Nucleus*

Author	Date	Movement	Pathologic Change
C. and O. Vogt [46]..... (cases 20, 21, 22)	1920	Spasms; athetoses	Degenerations of striatum and pallidum; alteration of subthalamic nucleus (decrease in size, poverty of capsule)
A. Jakob [1] (case 7)....	1923	Generalized gross choreiform movements	Senile changes in many regions, including subthalamic nuclei
Weil [56].....	1928	Choreiform movements of right arm and shoulder	Atrophy of striatum and pallidum; gliosis and pigmentation of neurons in subthalamic nuclei
Schroeder, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **23**: 431-510, 1914	1931	Choreiform jerkings of fingers, toes and shoulders	Huntington's disease; atrophy of subthalamic nuclei, gliosis and neuronal degeneration

In Balthasar's [22] first case the oral pole was chiefly destroyed, and here the face and the upper extremity were more severely affected than the lower extremity. Similarly, however, less severe involvement of the lower extremities was noted in most cases of the present series.

III. BALLISM WITH LESIONS ELSEWHERE

Ballism was described also (*a*) in 6 cases in which pathologic changes spared the subthalamic nucleus but interrupted what are presumed to be its connections, (*b*) in at least 2 cases in which pathologic

46. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen der striären Systems, J. f. Psychol. u. Neurol. **25**:627-846, 1920.

47. von Sántha, K.: Hemiballismus und Corpus Luysi: Anatomische und pathophysiologische Beiträge zur Frage des Hemiballismus nebst Versuch einer somatotopischen Lokalisation im Corpus Luysi, Ztschr. f. d. ges. Neurol. u. Psychiat. **141**:321-342, 1932.

48. Juba, A., and Rakonitz, E.: Ueber einen Fall von Hemiballismus (Beitrag zur Somatotopie des Corpus Luysi), Arch. f. Psychiat. **106**:629-642, 1937.

changes in the nucleus were part of a more generalized process and (*c*) in at least 4 cases in which no demonstrable change of the nucleus or connections was discerned. These reports will now be presented.

Pathologic Changes Interrupting Connections of the Subthalamic Nucleus.—Papez, Bennett and Cash [49] reported a case of hemiballism with lesions in the ipsilateral pallidum and the contralateral prerubral field, the subthalamic nuclei being intact. Although the fiber connections of the nucleus are not completely understood, at least some of its afferent fibers arise in the external segment of the pallidum, and some efferent fibers cross to the prerubral field in the subthalamic decussation. Their interruption is presumed to have caused the symptom in this case. In Kelman's [37] second case, although the tip of the oral pole of the nucleus was involved, the carcinomatous metastasis "was so placed as to affect essentially the subthalamicotegmental fibers," which constitute an ipsilateral efferent connection. Lewandowsky and Stadelmann [50] reported a case of a condition not clearly hemiballism by description, but with hemorrhagic softening of the retrolenticular portion of the internal capsule, extending somewhat into Forel's field. This lesion may have interrupted afferent fibers to the nucleus from the pallidum, which pierce the internal capsule in the region.

Balthasar [51] was inclined to attribute the ballism in his case to softening in the external segment of the contralateral pallidum and interruption of the subthalamic afferent fibers, although pathologic changes were present in both nuclei, being more extensive contralateral to the ballistic movements. Alexander [52] expressed the opinion that the latter changes deserved severer indictment, and placed the case with those of nonlocalized pathologic processes in which the nuclei take part. The metastasis in Bonhoeffer's case [12] and the tubercle in Bianchi's [53] were situated in the pons and involved the medial lemniscus; they may have been related to the hemichorea present though interruption of the descending subthalamicotegmental fibers as they pass caudad medial to this tract. The diagnosis of ballism may be inferred from

49. Papez, J. W.; Bennett, A. E., and Cash, P. T.: Hemichorea (Hemiballismus): Association with a Pallidal Lesion, Involving Afferent and Efferent Connections of the Subthalamic Nucleus; Curare Therapy, Arch. Neurol. & Psychiat. **47**:667-676 (April) 1942.

50. Lewandowsky, M., and Stadelmann, E.: Chorea apoplectica, Ztschr. f.d.ges. Neurol. u. Psychiat. **12**:530-539, 1912.

51. Balthasar, K.: Ueber die Beteiligung des Globus pallidus bei Athetose und Paraballismus, Deutsche Ztschr. f. Nervenh. **148**:243-261, 1939.

52. Alexander, L.: The Fundamental Types of Histopathologic Changes Encountered in Cases of Athetosis and Paralysis Agitans, A. Research Nerv. & Ment. Dis. Proc. **21**:389, 1942.

53. Bianchi, L.: Contributo alla conoscenza della emicorea sintomatica, Ann. di nevrol. **27**:1-42, 1909.

the description in Bonhoeffer's case, although in both cases the condition was reported as hemichorea.

These 6 cases constitute a suggestive, but not conclusive, body of evidence that hemiballism may be produced by lesions interrupting the connections of the subthalamic nucleus.

Nonlocalized Pathologic Changes in the Subthalamic Nucleus.—Ballism was reported in Balthasar's [51] case, already referred to, in which pathologic changes in the subthalamic nuclei were part of a diffuse process. His case, in which left hemiballism and, finally, paraballism were present, was characterized by widespread senile changes with softening of the external segment of the right pallidum and atrophy and senile alterations in the subthalamic nuclei, more particularly on the right. The Vogts [54] described what might be termed "holoballism," with *état fibreux* of the putamen and caudate nucleus and atrophy of the pallidum and subthalamic nucleus bilaterally. In Myslivecek's case, cited by Pelnář and Sikl,[55] there was bilateral chorea, which, according to the latter, was ballistic. Instead of the anticipated bilateral subthalamic hemorrhage, autopsy revealed cerebral atrophy and diffuse degeneration of neurons in the striatum, thalamus and subthalamic nuclei.

With these reports also belongs the case of Titica and Bogaert,[55a] characterized by monoballistic movements of the right upper extremity, the pathologic changes being diffuse and including extreme atrophy of the right subthalamic nucleus.

That such nonlocalized pathologic change in the subthalamic nucleus does not consistently evoke ballism was evidenced by the 6 cases in table 10, in which were presented a variety of involuntary movements, but not ballism. In the cases reported by Weil [56] and A. Jakob, ballism may have existed, but its presence could not be inferred from the clinical descriptions.

Hemiballism Without Pathologic Changes in the Subthalamic Nuclei or Their Connections.—In the clinicopathologic reports of the following cases, the clinical description of ballism can scarcely be in doubt, and the subthalamic nuclei and their connections were devoid of pathologic changes. Fragnito and Scarpini [57] reported such a case. After slight left hemiplegia and transient "psychomotor agitation," a laborer aged

54. Vogt and Vogt,[46] p. 709.

55. Pelnář and Sikl,[36] p. 331.

55a. Titica, J., and van Bogaert, L.: Heredo-Degenerative Hemiballismus; a Contribution to the Question of Primary Atrophy of the Corpus Luysi, Brain **69**:251-263, 1946.

56. Weil, A.: A Contribution to the Pathology of Hemichorea, Brain **51**:36-45, 1928.

57. Fragnito, O., and Scarpini, V.: Reperto anatomopathologico in un caso di emicorea sintomatica, Riv. di pat. nerv. **31**:524-531, 1926.

80 exhibited "choreic excitation" of the upper and lower extremities on the left side, with particular involvement of the deltoid muscle and "expansive" movements, which persisted more than three years. At a carefully reported autopsy, lacunar softenings of the head of the caudate nucleus and the internal portion of the putamen, as well as an insignificant, pea-sized softening in the medial nucleus of the optic thalamus, were observed contralaterally. In answer to Martin's question,[19b] Fragnito specifically denied the presence of pathologic changes in the corpus Luysi, Forel's field and the medial lemniscus.

In Wilson's [58] case there developed typical right hemiballism,[59] which persisted and progressed for eleven years, until it was necessary to fashion an iron frame to protect the patient, an old woman, from the blows of her own arm. Autopsy revealed atrophy of the left postcentral gyrus as the sole lesion. Careful histologic study failed to disclose any pathologic changes in the basal ganglia, and Wilson's statement on the condition of the subthalamic nucleus was pointed and emphatic: ". . . no alterations of any kind among the cells or fibers; they were normal."

Austregesilo and Borges Fortes [60] reported the case of a woman aged 32 who showed ballistic movements of the left side after three attacks of apoplexy—"movements of the limbs, which were rapid, violent, spasmodic and disorderly, being principally hyperextensions (hemiballism)." Cortical softening was observed in the island of Reil, but no pathologic changes were discovered in the subthalamic region.

Rothfield and Demianowska [61] reported a case of hemiballism in which the subthalamic nuclei were intact. Lesions were described, however, in the contralateral internal capsule and neostriatum, and it is conceivable that the former may have interrupted fibers to the nucleus.

Dunlap [62] described involuntary movements of the whole body, but especially of the upper extremity—"coarse, awkward, and of wide excur-

58. Wilson, S. A. K.: Die Pathogenese der unwillkürlichen Bewegungen mit besonderer Berücksichtigung der Pathologie und Pathogenese der Chorea, Deutsche Ztschr. f. Nervenh. **108**:4-38, 1929.

59. Wilson's description [58] (page 16) is striking: "It [the symptom] consisted of wild choreiform movements of the arm, limited to the right side, and affecting the larger joints much more markedly than the smaller ones. The arm was flung about in all directions, and struck the patient and those who came unknowingly into her vicinity; it was thrown around against pieces of furniture."

60. Austregesilo, A., Jr., and Borges Fortes, A.: Étude anatomo-clinique d'un cas d'aphasie de Wernicke avec hémiballisme, Rev. sud.-am. de méd. et de chir. **2**: 1111-1124, 1931.

61. Rothfield, J., and Demianowska, M.: Przyczynek do patogenezy hemibalizmu, Polska gaz. lek. **15**:569-575, 1936 (German summary, p. 574).

62. Dunlap, C. B.: Pathologic Changes in Huntington's Chorea, with Special Reference to the Corpus Striatum, Arch. Neurol. & Psychiat. **18**:867-943 (Dec.) 1927.

sion"; hence, presumably ballistic in a woman aged 63 with Huntington's disease (hereditary chronic progressive chorea) (case 938, page 937); he noted no particular changes in the subthalamic nuclei in this case or in any other cases of the disease which he studied. Both Wenderowic [20] and Martin [19b] asserted they had seen ballistic movements in patients with Huntington's disease. Davison and Goodhart [63] described ballistic movements in a case of dystonia musculorum deformans; besides scattered lesions in the cerebrum, they noted that the capsule of the subthalamic nucleus was lightly stained. Finally, Sydenham's chorea is a hemichorea in many cases (almost 50 per cent, according to Wilson [64]); ballistic movements may be observed in many such cases, and no consistent changes in the subthalamic nucleus have been recognized.

Fundamentally dissimilar symptoms may become confused in the process of written description. It is entirely possible that a comparison of motion picture records, were they available, would necessitate a reclassification of these and other cases, and perhaps set hemiballism apart as a symptom unrelated to any pathologic changes other than those of the subthalamic nucleus. But it appears inescapable that in at least 3 cases (Fragnito and Scarpini [57]; Wilson,[58] and Austregesilo and Borges Fortes [60]) hemiballism existed without demonstrable pathologic change in this structure.

Miscellaneous Clinicopathologic Cases.—A number of cases might be included with the 30 cases with localized lesions were it not for inadequacies in the clinical description or pathologic report. Pette [65] reported a case in which a pea-sized neoplastic metastasis appeared in the "regio subthalamica," and Spatz,[66] a case in which a fresh hemorrhage destroyed the subthalamic nucleus and involved the internal capsule. The lesion in Pette's case was associated with what was probably hemiballism ("a severe choreiform disturbance of the whole left side of the body"), and that in Spatz's case, with hemiballism by name only. Schaffer [67] reported a case as one of hemiballism ("violent massive movements") with hemorrhage limited to the contralateral subthalamic nucleus. Kulenkampff [34] recorded a case of monoballism of the right upper extremity of three years' duration, in which autopsy showed scarring and atrophy of cells in the lenticular nucleus and, "even macro-

63. Davison, C., and Goodhart, S. P.: Dystonia Musculorum Deformans: A Clinicopathologic Study, Arch. Neurol. & Psychiat. **29**:1108-1124 (May) 1933.

64. Wilson,[17] p. 617.

65. Pette, H.: Zur Localization hemichoreatischer Bewegungsstörungen, Zentralbl. f.d. ges. Neurol. u. Psychiat. **30**:407-408, 1922.

66. Spatz, H.: Anatomische Abteilung, Arch. f. Psychiat. **80**:279, 1927.

67. Schaffer, K.: Ueber Hemiballismus, klinisch und anatomisch, Zentralbl. f. d. ges. Neurol. u. Psychiat. **49**:847, 1928.

scopically, an atrophy of the basal nuclei in the region of the internal capsule." In Bertrand and Christophe's [27] case, reported as one of hemiballism, a hemorrhage involving essentially the contralateral subthalamic nucleus extended also into the substantia nigra and the capsule of the red nucleus. The evaluation of this case is difficult because of the meager pathologic report and the rather major psychic symptoms.

There are at least 5 cases which may not be classified without further reservations. A case of Souques and Bertrand,[68] reported as one of hemichorea, was characterized by choreoathetotic movements of the left side, which dislocated the shoulder by their violence. They had persisted for fifty years, having their onset with post-typhoid hemiplegia at the age of 4 years. Softenings of the contralateral caudate nucleus, putamen and external segment of the pallidum were observed, with extreme atrophy of the subthalamic nucleus on that side. The case may belong with those having interruption of the connections of the nucleus. In Nikitin's [69] case, postapoplectic hemiballism involving the right side of a patient aged 77 was associated with hemorrhage in the left thalamus, which, as von Sántha stated, "approached within 2 mm. of the dorsal border of the intact subthalamic nucleus." In Hampel's [70] case, reported as one of hemiballism with a syphilitic basis, gliosis and neuronal degeneration were observed in the putamen and the subthalamic nucleus, being more extensive in the latter contralateral to the ballistic movements, but major psychic symptoms suggested a cautious evaluation. In case 3 of Marcus and Sjögren,[71] that of a woman aged 88 who died of bronchopneumonia twelve months after onset of hemiballism involving the right side, strip-shaped softenings, present bilaterally, involved the thalamus, subthalamic nucleus, internal capsule and a portion of the pallidum contralateral to the ballistic movements, and the same structures on the right except for the subthalamic nucleus.

Whether the involuntary movements shown by Lloyd and Winkelman's [72] patient were ballistic was not clear from the description; a recent hemorrhage on the opposite side destroyed portions of the striatum and the internal capsule and "impinged on the corpus Luysi."

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68. Souques, A., and Bertrand, I.: Sur la fonction motrice du corps strié, à propos d'un cas d'hémichorée suivi d'autopsie, Rev. neurol. **33**:988-1002, 1926.

69. Nikitin: Zusammenfassungen internationaler Neurologenkongress zu Bern, 1932; cited by von Sántha [47] (p. 331).

70. Hampel, E.: Hemiballismus auf luischer Grundlage: Beitrag zur pathologischen Anatomie und Pathogenese des Hemiballismus, Deutsche Ztschr. f. Nervenh. **141**:77-96, 1936.

71. Marcus and Sjögren,[30] p. 18.

72. Lloyd, J. H., and Winkelman, N. W.: A Case of Acute Posthemiplegic Choreiform Movements on the Unparalyzed Side: Study of the Basal Ganglia, Am. J. M. Sc. **169**:247-253, 1925.

Finally, Kashida's [73] case (page 696) combined athetosis, torsion dystonia and hemiballism with a multiplicity of pathologic changes, among which was a diminution in size and absence of capsular fibers of the subthalamic nucleus.

Clinical Cases Without Autopsy.—Some kind of localized change in the subthalamic nucleus seems to have been present with ballism in the clinical cases of Grigoresco and Axente,[74] Marcus and Sjögren [30] (cases 4 and 5) and von Angyal and von Pethe.[75] The probable pathologic changes were, respectively, hemorrhage, gumma, embolus and syphilitic necrosis. The probable pathologic lesions were more or less obscure in the cases of Jermutowicz,[33] Rakonitz, [76] Alurralde and Sepich,[77] Urechia and Bumbacescu, [78] Bauman,[79] and Teske.[80]

SUMMARY AND CONCLUSIONS

A review of the literature disclosed 30 cases of hemiballism associated with localized pathologic change in the subthalamic nucleus. Analysis of these cases led to the following conclusions:

1. Ballism is a distinct form of involuntary movement characterized by continuous, violent, coordinated activity of the axial and proximal appendicular musculature such that the limbs are flung about.

2. Hemiballism, and sometimes monoballism of the upper extremity, is the apparently inevitable symptom in man of destruction localized in the contralateral subthalamic nucleus (nucleus hypothalamicus; corpus Luysi).

3. There is evidence that interruption of the connections of the subthalamic nucleus may result in hemiballism.

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73. Kashida: Ueber Gehirnarteriosclerose des früheren Alters und über die Kombination von corticalen, pyramidalen und extrapyramidalen Symptomen bei der Gehirnarteriosclerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:659-702, 1925.

74. Grigoresco, D., and Axente, S.: Syndrom Luysien: Influence du tabac sur les grands mouvements d'hémiballisme, Rev. neurol. **1**:361-363, 1931.

75. von Angyal, L., and von Pethe, F.: Ein Fall von Monoballismus luischer Genese, Arch. f. Psychiat. **113**:120-125, 1941.

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4. Hemiballism may appear without demonstrable pathologic change in the subthalamic nucleus or its connections, although such cases are relatively rare.

5. Ballistic movements may appear in a variety of dyskinesias, to which the relation of the subthalamic nucleus is as yet obscure. Their similarity to or identity with those of hemiballism following damage to the subthalamic nucleus awaits a more complete, and preferably cinematographic, comparison.

6. Adequate clinical description and pathologic study will continue to be of value in elucidating the genesis and nature of this remarkable symptom.

630 West One Hundred and Sixty-Eighth Street.

ELECTROENCEPHALOGRAPHIC STUDIES ON INDUCED AND EXCISED EPILEPTOGENIC FOCI IN MONKEYS

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LENORE M. KOPELOFF, Ph.D.
AND
NICHOLAS KOPELOFF, Ph.D.
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PREVIOUSLY we [1] reported that the experimental production of epilepsy in the monkey was associated with electroencephalographic abnormality. It was noted that in addition to a primary focus in the region of application of the inciting agent, there was evidence of spread of electroencephalographic abnormality to the opposite side of the brain.[2]

PRESENT INVESTIGATION

The present study is concerned with more detailed observations regarding the time relation between electroencephalographic evidence of primary and secondary foci and the onset of convulsive seizures. In addition, the effect of ablation of the "active" focus was investigated.

Technic.—In accordance with the method previously described,[1a] unilateral application of hydrous oxides of aluminum to the motor cortex of 4 monkeys resulted in epileptiform seizures in every instance on physical stimulation. As controls, 3 additional monkeys similarly prepared with noneffective materials at no time manifested convulsive seizures. Electroencephalographic records were taken before operation and at intervals thereafter. A head control apparatus attached to an animal board and a bandage over the eyes aided in immobilizing the animal. Curare [3] was administered intravenously when necessary in doses approximating 1 mg. per kilogram of body weight. This dose of curare was without apparent effect on the electroencephalographic pattern. Electroencephalograms were taken with a two channel Rahm machine, utilizing a bipolar system

From the Departments of Experimental Psychiatry and Bacteriology, New York State Psychiatric Institute and Hospital.

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TABLE 1.—*Electroencephalographic and Clinical Observations on Monkeys with Induced and Excised Epileptogenic Foci*

Active Substance *—Alumina Cream [4]

Animal 449					Animal 450					Animal 451					Animal 452				
	Electroencephalogram †		Seizures ‡			Electroencephalogram		Seizures			Electroencephalogram		Seizures			Electroencephalogram		Seizures	
Weeks	Left	Right	Left	Right	Weeks	Left	Right	Left	Right	Weeks	Left	Right	Left	Right	Weeks	Left	Right	Left	Right
0¾	±	±	0	0	0	0	0	0	0	0	..	..	0	0	0	..	..	0	0
5	++	±	0	0	6	+	0	0	0	5¶	+	±	0	0	5	+	±	0	0
7¶	..	..	S	0	8	+±	±	0	0	7¶	+	±	0	0	8	++	+±	S	0
13	++	+	S	0	13	++	+	0	0	11	+	±	0	0	11	++	+	0	0
24	++	+	S	0	22	+	±	S	0	12	..	..	S	S	20	..	..	0	0
38	++++	++	S	0	28	++	+±	..	..	20	..	..	S	S	24	+++	++	..	..
39	..	..	S	S	37	+++	++	S	0	24	++	+	S	S	31	++	+±	S	S
45	+++	+±	S	S	39	+++	++	S	S	27	+++	++±	S	S	36	+++	++	S	S
46	..	..	S	0	61	+++	++±	S	S	34	+++	++	S	S	40	+++	++	S	S
62	+±	+	S	0						35	++	+	S	0	53	+++	++	S	S
63	..	..	S	0						35½	Ablation left area [4]				54½	Ablation left area [4]			
65	..	..	0	0						36	±	+	S	S	55	+±	+	0	0
73	+++	+±	S	0						37	++	+	S	S	57	+	+	0	0
77	++	+±	S	0						39	+	+	0	0	58	..	..	0	0
81	++	+±	0	0						41	+	±	0	0	60	+	±	0	0
82	++	+	S	0						43	+	±	S	S	63	+	±	0	0
										46	+	±	S	0					
										48	±	0	0	0					
										50	±	0	0	0					
										52	+	0	0	0					
										63	0	0	0	0					

Control Substances *

Rare Earth Oxides

Animal 453					Animal 454				
	Electroencephalogram		Seizures Opposite			Electroencephalogram		Seizures Opposite	
Weeks	Left	Right	Left	Right	Weeks	Left	Right	Left	Right
0	..	..	0	0	0	..	..	0	0
4	0	0	0	0	4	0	0	0	0
6	0	0	0	0	6	0	0	0	0
28	0	0	0	0	28	0	0	0	0
35	0	0	0	0	35	0	0	0	0
39	0	0	0	0	39	0	0	0	0
43	0	0	0	0	43	0	0	0	0
61	0	0	0	0	45	0	0	0	0
78	0	0	0	0	61	0	0	0	0

Zinc Oxide

Animal 430				
	Electroencephalogram		Seizures Opposite	
Weeks	Left	Right	Left	Right
0	..	..	0	0
71	0	0	0	0
72	Ablation left area [4]			
72½	±	0	0	0
73	0	0	0	0
75	0	0	0	0
79	0	0	0	0
81	0	0	0	0
116	0	0	0	0
122	0	0	0	0

* The agent was applied to the left motor cortex.

† Left and right indicate leads from the left and right side of the cortex. The signs ± to ++++ represent increasing degrees of electroencephalographic abnormality, as indicated by the incidence and duration of delta waves, sharp formations and spike potentials.

‡ S indicates seizure; 0, no seizures.

§ Before operation.

of recording. The electrodes consisted of needle clips firmly affixed to the scalp over the prefrontal, motor and occipital regions of both sides of the head. Electroencephalographic abnormalities were classified as slight, moderate and severe, depending on the frequency rate and incidence of slow activity, the irregularity of pattern and the amount of high voltage fast activity.

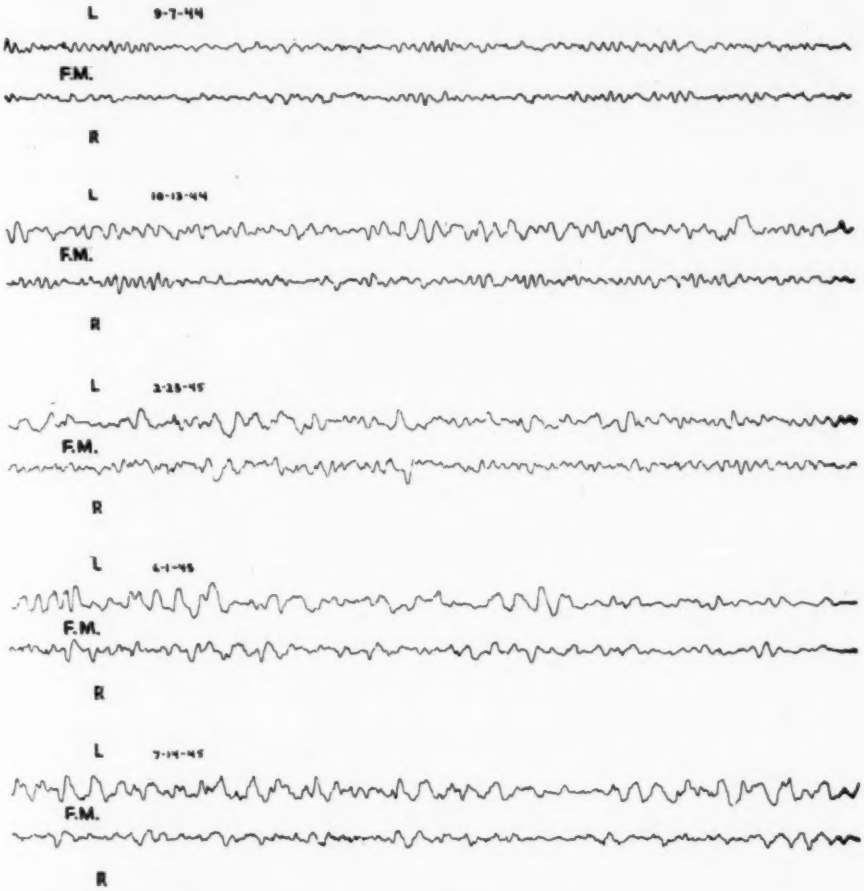

Fig. 1 (monkey 449).—*9/7/44:* Control tracing prior to operation, taken with bilateral frontomotor leads (*F.M.*) showing normal activity with frequent trains of alpha rhythm.

10/13/44: Five weeks after application of the active agent to the left precentral cortex. No clinical seizures occurred. The tracing from the left frontomotor (*F.M.*) lead shows irregular delta activity.

2/23/45: Twenty-four weeks after operation. Contralateral seizures were elicited. Abnormal electroencephalographic activity is present bilaterally, being predominant on the left side.

6/1/45: Thirty-eight weeks after application of the agent, or one week preceding onset of generalized convulsions. Electroencephalographic abnormality is increased, being more pronounced on the left.

7/14/45: Forty-five weeks after application of the agent. Generalized convulsions were present. The tracing shows pronounced abnormality, especially persistent on the left, with a greater incidence of sharp formations.

* The agent was applied to the left motor cortex.
† Left and right indicate leads from the left and right side of the cortex. The signs + to ++++ represent increasing degrees of electroencephalographic abnormality, as indicated by the incidence and duration of delta waves, sharp formations and spike potentials.
‡ ‡ Indicates seizure; 0, no seizures.
§ During observation.

Observations.—The clinical and electroencephalographic observations are recorded in table 1, and representative electroencephalograms are shown in figures 1 and 2. It may be seen in general that within five weeks after operation the electroencephalogram revealed a focus of abnormality consisting chiefly of delta activity, random spikes and sharp formations about the site of application of the alumina cream.[4] At the same time, or shortly thereafter, abnormality in the electroencephalo-

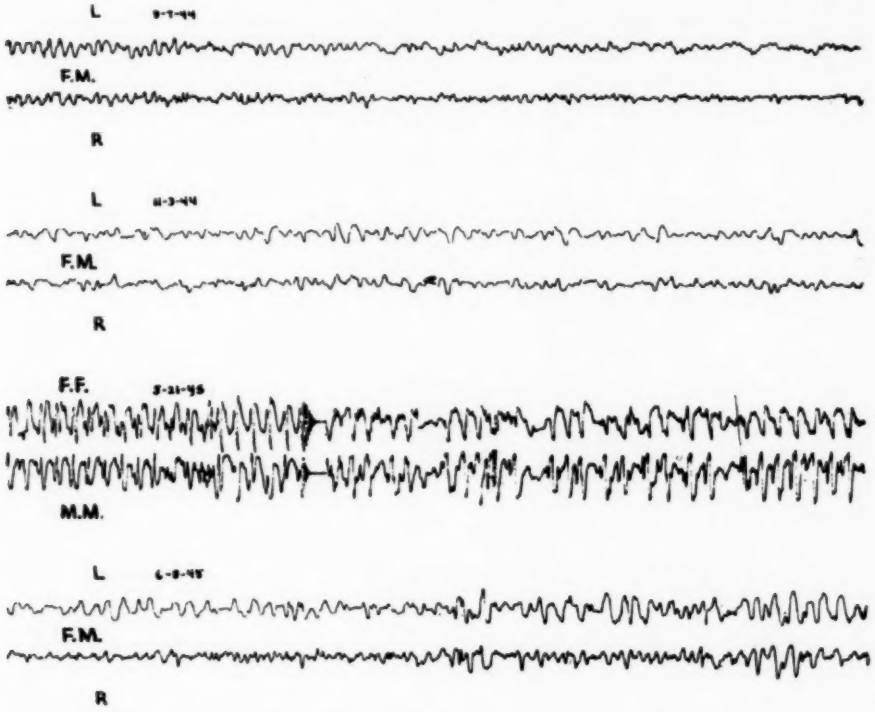

Fig. 2 (monkey 450)—*9/7/44:* Control tracing prior to operation, taken with bilateral frontomotor leads (*F.M.*), showing normal activity, with frequent trains of alpha rhythm and some low voltage fast activity.

11/3/44: Eight weeks after application of the active agent to the left precentral cortex. No clinical seizures were observed. The left frontomotor (*F.M.*) lead shows irregular delta activity; the right, irregular features and occasional slow waves.

5/21/45: Thirty-seven weeks after application of the agent, and two weeks preceding onset of generalized convulsions. Contralateral seizures were elicited. The transfrontal (*F.F.*) and frontomotor (*M.M.*) leads show frequent bursts of spike and dome activity.

6/8/45: Thirty-nine weeks after operation. General convulsions occurred. Abnormal activity (delta waves and random spike potentials) is present, being more pronounced on the left. Discharges of spike and dome activity are not present, but frequent trains of serial slow rhythm are noted.

4. "Alumina cream was prepared by adding a slight excess of 1 per cent solution of ammonium hydroxide at room temperature to a 1 per cent solution of ammonium alum (ammonium aluminum sulfate) and the resulting precipitate washed by decantation until only traces of sulfate remained in the supernatant fluid." [1a]

graphic pattern appeared in the corresponding region of the opposite side. These abnormalities increased in degree for a number of months and usually reached a maximum in twenty-four weeks. In 1 instance this occurred in seventy weeks and in another in two hundred and thirteen weeks. Although increasing electroencephalographic abnormality was noted on both sides, it was relatively greater on the side of application of the inciting agent. In 2 monkeys the abnormality had become approximately the same on the two sides after fifty-four and sixty-one weeks, respectively. The maximal electroencephalographic disturbance persisted for varying periods, from three to twenty-nine weeks, in 4 monkeys (449, 450, 451 and 452) on which extended observations were made. In control animals (453 and 454) to which rare earth oxides, instead of aluminum compounds, had been applied, clinical seizures could not be elicited, and electroencephalograms revealed no abnormalities during the sixty-one week period of observation (fig. 3).

A relationship between electroencephalographic abnormality and the manifestation of convulsive seizures may be seen from the data in table 1. In all monkeys electroencephalographic abnormality preceded the onset of seizures. With minimal disturbances in the electroencephalogram, seizures were almost always confined to one side of the body. With increasingly abnormal electroencephalographic activity, convulsions became generalized and could readily be elicited over a period of several months. When the electroencephalographic abnormality decreased, the seizures were confined to one side. In 1 instance (monkey 449) in which occasional seizure-free periods occurred, evidence of focal abnormality was still present.

The effect of ablation of a focus induced by alumina cream was studied in 2 monkeys (451 and 452). Generalized convulsions had been elicited by physical stimulation over a period of twenty-three and twenty-two weeks, respectively, after which the disks were removed and area 4 of the original focus was ablated by cauterization (monkey 451) or suction (monkey 452). During the succeeding seven weeks generalized convulsions were elicited intermittently in monkey 451. At the end of the tenth week contralateral jacksonian seizures only were observed. Subsequently, no convulsive manifestations could be induced. During the postablation period the electroencephalogram showed a gradual diminution in the degree of abnormality, with only slight delta activity in the region of the original focus after the tenth week. By the twenty-seventh week delta waves had disappeared (table 1 and fig. 4). In monkey 452, no convulsive manifestations could be elicited after ablation, despite a generally abnormal electroencephalographic record. Within six weeks after ablation the electroencephalogram showed gradual diminution and eventual disappearance of delta activity. It should be stated that in monkey 452 the ablation was extended beyond area 4

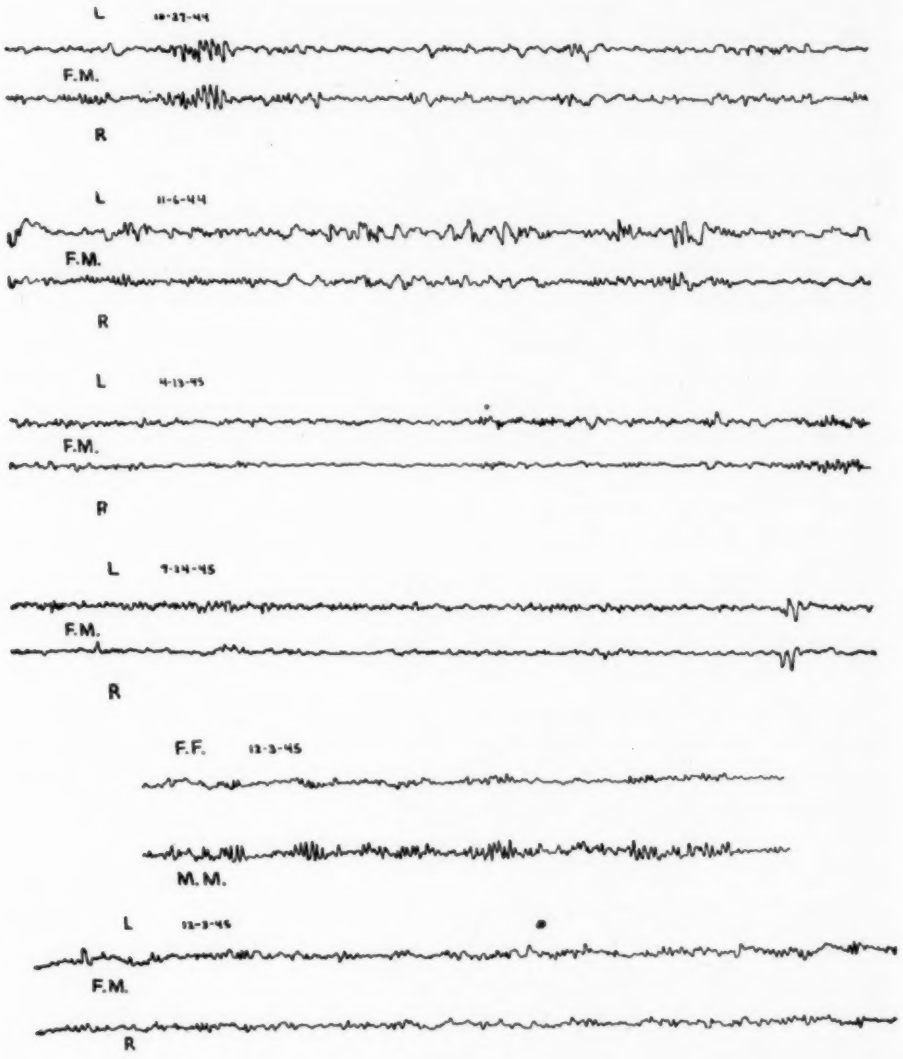

Fig. 3 (monkey 454; control animal).—*10/27/44:* Four weeks after application of an inactive agent (rare earth oxides) to the left precentral cortex. No clinical seizures were present. There are no electroencephalographic abnormalities or significant differences between the two sides.

11/6/44: Six weeks after application of the inactive agent. No seizures were elicited. The electroencephalographic pattern is similar to that shown in the preceding tracing.

4/13/45: Twenty-eight weeks after application of the agent. No seizures were observed. No electroencephalographic abnormalities are present.

7/24/45: Forty-three weeks after operation. There were no seizures. No electroencephalographic abnormalities are present.

12/3/45: Sixty-one weeks after operation. No seizures occurred. No electroencephalographic abnormalities or significant differences between the two sides are observed.

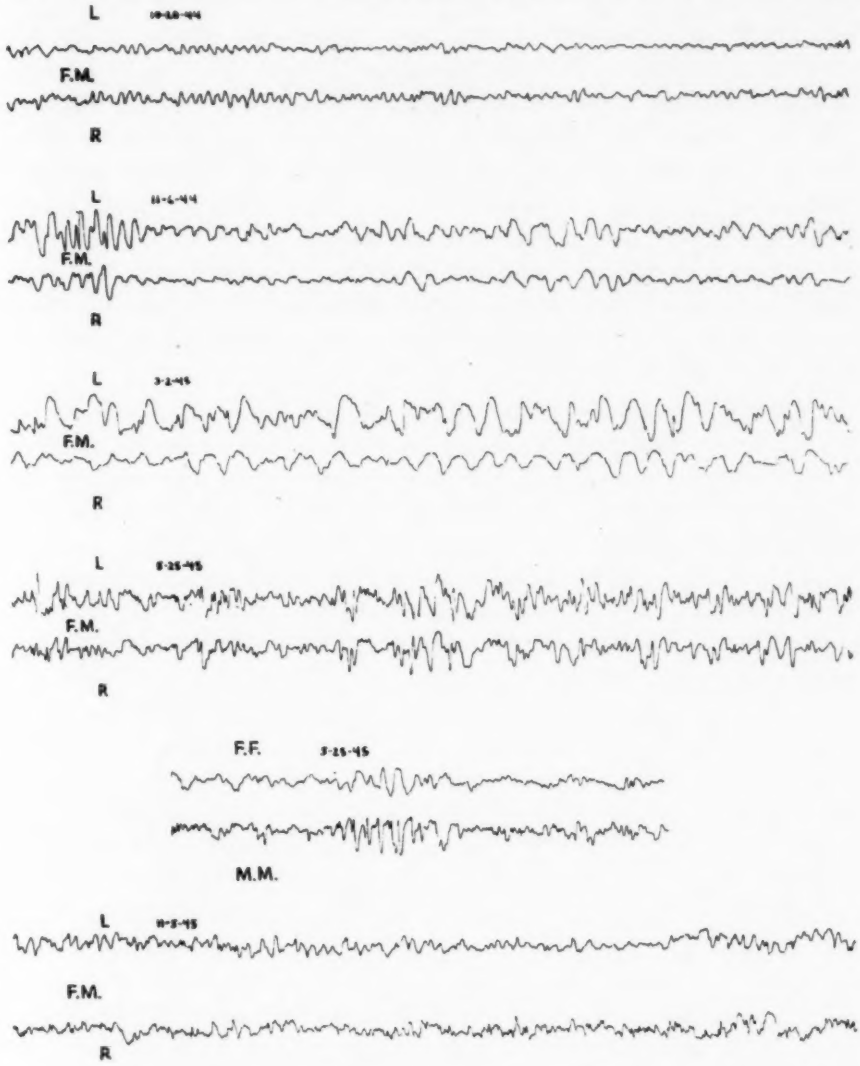

Fig. 4 (monkey 452).—*10/20/44:* Tracing five weeks after application of the active agent to the left precentral cortex. There were no clinical seizures. Beginning electroencephalographic disturbances are obtained from the left side.

11/6/44: Eight weeks after operation. Contralateral seizures were elicited. Frequent bursts of slow activity and spike and dome discharges appear on the left. Bursts of slow activity are also present on the right, with relatively diminished amplitude, but no spike potentials.

3/2/45: Twenty-four weeks after operation, and seven weeks before generalized seizures were observed. Frequent serial delta activity is present on the left, with random spike potentials. Serial slow activity, of lower amplitude and without spike formation, is present on the right.

5/25/45: Thirty-six weeks after operation. Generalized convulsions were present. Increased fast activity, frequent spike potentials and random spike and dome complexes are present bilaterally, being more pronounced over the left precentral cortex.

11/5/45: Sixty weeks after application of the active agent, or five and one-half weeks after ablation of area 4 of the left side. No clinical seizures occurred after ablation. The electroencephalographic disturbance is greatly decreased, with frequent trains of alpha rhythm, occasional slow potentials and low voltage sharp formations.

into area 6 approximately 1 mm. and the anterior border of the postcentral gyrus undermined approximately 2 mm. This more extensive ablation may have removed more motor cells and more of the focal zone than was ablated in monkey 451, and may well account for the abrupt cessation of seizures and the more rapid diminution of abnormal electroencephalographic activity in this monkey. In a control animal (monkey 430), which had received applications of zinc oxide to the left motor cortex, with no convulsive manifestations, for seventy-two weeks, the disk was removed and area 4 electrocauterized. The electroencephalogram showed no persisting abnormality either one week before or forty-three weeks after cauterization (fig. 5).

It seemed of interest to determine whether any significant differences in convulsive reactivity to metrazol existed between animals exhibiting chronic convulsive seizures and others which had been similarly prepared with nonepileptogenic materials. A further comparison was made with monkeys of both types in which ablation of area 4 had been performed. Also included were 1 monkey in which alumina cream had been applied to the area underlying the ablated motor cortex, 1 monkey in which only areas 4 and 6 on one side had been ablated, and 6 monkeys without operation. Clinical epileptic seizures had never been elicited in the monkeys prepared with nonepileptogenic substances or after surgical ablation of the previously treated motor cortex. Intravenous injections of 10 per cent metrazol were administered to each monkey in graduated daily doses until the limiting convulsant dose was established. The results are presented in table 2. It may be seen that in all animals in which alumina cream had been applied to the precentral cortex or to the underlying subcortical tissue, the limiting convulsant dose of 10 per cent metrazol was below 0.25 cc. Similar results were obtained in those monkeys which had received alumina cream over the precentral cortex and in which the subsequent ablation of the treated area had resulted in cessation of convulsive seizures. However, it is likely that some alteration of the cellular elements (motor cells outside area 4) surrounding the original focal zone or the area of ablation may have been responsible for the persistence of the lowered threshold observed. More extensive ablations into the prefrontal and anterior parietal zones are contemplated. The critical convulsant dose of metrazol for the 3 monkeys prepared with nonepileptogenic substances (in 1 of which the motor cortex had been ablated), or for the animal in which only ablation of the motor cortex had been performed, or for untreated monkeys was found to be between 0.4 and 0.6 cc. Therefore, it is evident that alumina cream caused a lowering of the convulsive threshold to metrazol even when clinical seizures had been eliminated or prevented by surgical ablation of the precentral cortex.

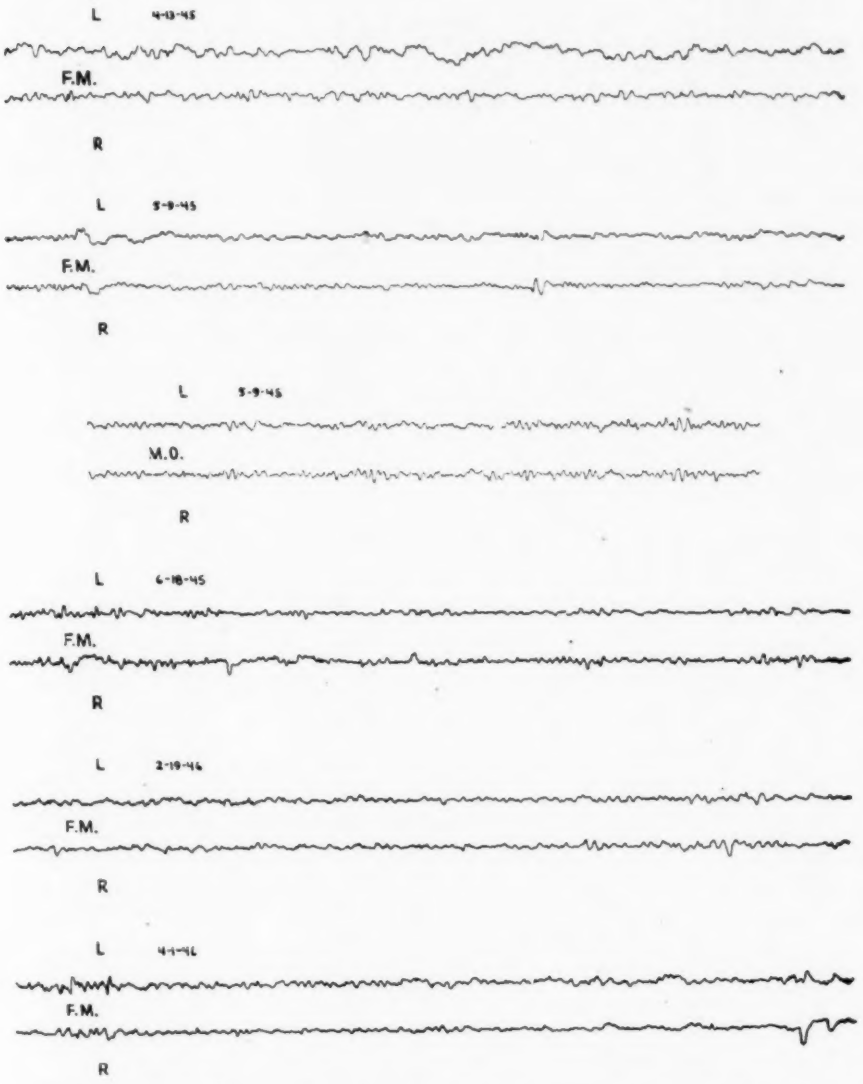

Fig. 5 (monkey 430, control animal).—Tracing seventy-one weeks after application of an inactive agent (zinc oxide) to the left precentral cortex. No clinical seizures were observed. Ablation of area 4 of the left side was performed on April 20.

5/9/45: Seventy-five weeks after application of the agent, and three weeks after ablation. No seizures were observed. No electroencephalographic abnormalities are present (*M.O.* indicates motor occipital area).

6/18/45: Eighty-one weeks after application of the agent, and nine weeks after ablation. No seizures were observed. No electroencephalographic abnormalities are present.

2/19/46: One hundred and sixteen weeks after application of the agent and forty-four weeks after ablation. No seizures were observed. No electroencephalographic abnormalities are present.

4/1/46: One hundred and twenty-two weeks after application of the agent, and fifty weeks after ablation. No seizures were observed. No electroencephalographic abnormalities are present.

TABLE 2.—*Critical Convulsant Dose of 10 per Cent Metrazol*

Monkey No.	Date	First Operation	Date	Second Operation	Convulsive Seizures	Minimal Intravenous Convulsant Dose of Metrazol, Cc.*
		Epileptogenic Material				
449	9/ 8/44	Alumina cream,[4] motor cortex	.....		+	0.05†
457	1/10/45	Alumina cream,[4] motor cortex	.....		+	0.20
451	9/15/44	Alumina cream,[4] motor cortex	5/16/45	Ablation of motor cortex	+‡	0.25
452	9/15/44	Alumina cream,[4] motor cortex	10/ 2/45	Ablation of motor cortex	+‡	0.15
420	11/23/43	Ablation of motor cortex; alumina cream applied subcortically	.....		..§	0.20
		Nonepileptogenic Material				
453	9/29/44	Rare earth oxides, motor cortex	.....		0	0.50
454	9/29/44	Rare earth oxides, motor cortex	.....		0	0.50
430	11/30/43	Zinc oxide, motor cortex	4/18/44	Ablation of motor cortex	0	0.60
487	12/ 4/45	Ablation of motor cortex	.....		0	0.50
		Controls Not Operated On				
496	.....				0	0.50
497	.....				0	0.60
500	.....				0	0.40
502	.....				0	0.40
503	.....				0	0.60
504	.....				0	0.40

* The minimal convulsant dose of 10 per cent metrazol, the approximate threshold value, was determined after repeated trials (April 22 to June 7, 1946).
† Lowest dose tested.
‡ Before ablation.
§ One short clonic seizure of the right leg only (March 14, 1944).

SUMMARY

1. In rhesus monkeys the application of alumina cream to the motor cortex on one side produced a primary focus of electroencephalographic abnormality, characterized chiefly by delta activity, random spikes and sharp formations. This abnormality appeared prior to the onset of jacksonian attacks, which could be elicited by physical stimulation. Subsequently, a secondary (mirror) focus of electroencephalographic abnormality developed in the opposite motor cortex, which was followed later by generalized convulsions.

2. A direct correlation was found between the degree of electroencephalographic abnormality and the convulsive threshold. Maximal electroencephalographic disturbance was usually associated with generalized convulsions. Minimal electroencephalographic abnormality was associated with jacksonian attacks and was also present after the cessation of seizures.

3. Ablation of area 4 resulted in eventual cessation of seizures and diminution of electroencephalographic abnormalities.

4. The limiting intravenous convulsant dose of metrazol for monkeys exhibiting epileptic seizures, or for similarly prepared monkeys after ablation of the primary focus, or for a monkey in which alumina cream had been applied subcortically, was significantly lower than that for control monkeys.

Miss Mary Szczerba, Mr. Benjamin Blattberg, Miss Judith Darmstadter and Mr. Kurt Lopez gave technical assistance.

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INVESTIGATIONS ON NARCODIAGNOSIS

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ONE of the essential problems in psychopathology is that of differentiation between primary and secondary determinants of abnormal mental states. Reduction of various clinical symptoms to a point where one group of characteristics finally emerges as the supposedly specific pathologic nucleus of a clinical entity led to the development of the concept of the "fundamental disturbance." Bleuler,[1] representing the Swiss school; Berze,[2] Birnbaum,[3] Küppers [4] and Kronfeld,[5] the German school, and Minkowski [6] and Claude,[7] the French school, are the main investigators of this subject. It was Claude who, in 1924, reported a new method which he believed to be experimental and objective. He selected negativistic schizophrenic patients, anesthetized them with ether and observed the changes in attitude which some of the patients displayed as they passed from consciousness into a state of narcosis. He concluded that patients who showed no changes at all suffered from a physiogenic disturbance, whereas patients who started to talk and respond had a psychogenic disturbance. In a way, this method can be called a forerunner of the sodium amytal interview. The differences between Claude's etherization method and the intravenous use of barbiturates are pharmacologic as well as conceptual. Claude intended to study the structure of psychoses in regard to determinants,

Read at the annual convention of the American Psychiatric Association, Chicago, May 28, 1946.

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which he conceived to be either organic or psychogenic. The question arises how the more perfected use of the narcotic method of today can be utilized for investigations into the structure of psychopathologic states.

Psychopharmacologic studies with sodium amytal by Lindemann,[8] Thorner [9] and others have revealed that the effect of the drug is anti-inhibitory. The interpretation of revealed contents depends essentially on concepts of personality structure. There is general agreement on the existence of forces within the personality which are not in the sphere of consciousness. Considerable diversity of opinion exists in regard to the nature of these forces. The problem of personality structure has a direct bearing on the utilization of the sodium amytal method. Lorenz [10] and Bleckwenn [11] reported observations on catatonic patients who while under the influence of sodium amytal showed changes from negativistic to responsive attitudes. These authors concluded that the psychosis, while being at a much lower level of mental existence than the normal, was not as deep as real unconsciousness. Precipitation into unconsciousness, therefore, would pierce through the level of catatonic stupor and dislodge the catatonic mechanism. Gottlieb and Hope [12] found sodium amytal to be a distinct aid in evaluation of the prognosis. They estimated the degree of preservation of personality by the extent to which the patient's behavior, under the influence of the drug, approached normal. The goal of the sodium amytal method becomes the uncovering of the more intact portions of the ego. These concepts, however, meet with certain difficulties. A schizophrenic patient, for instance, whose catatonic rigidity and mutism disappear under the influence of the drug does not really approach normal, but remains just as unrealistic and autistic in his general orientation as before. One must conclude, therefore, that the pathologic process affects the entire personality rather than isolated levels. It is this situation which necessitates differentiation between fundamental factors, an autistic and unrealistic orientation, for instance, and secondary phenomena, such as motor disturbance and mutism. Rigid concepts, dividing the personality into

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certain strata, interfere with maintaining the perspective of the total personality, especially in the case of pathologic changes which are fundamental and affect the personality in its entirety.

The aim of the present investigation is to study the qualitative aspects of the responses for a phenomenologic evaluation of determinants of symptom formation. For the purpose of this investigation, I shall advance a definition of these phenomena according to which fundamental factors express themselves as pathologic tendencies in general personality function, whereas secondary phenomena are to be attributed to subjective inner experiences. The interrelationship of these phenomena will be examined in the light of the actual observations, and interpretations will be based on the facts as they present themselves.

REPORT OF STUDY

The 56 patients selected for this investigation had previously been under my observation. Their behavior pattern as well as their past and present problems had been studied carefully. Thorough knowledge of a patient's personality must be considered a prerequisite for this use of the narcotic method, as it is otherwise impossible to gain an accurate impression of changes which occur in the state of altered consciousness.

Although it would be desirable to consider each patient individually, the brevity of this report demands that observations be classified according to types of responsivity. The common denominator of each response group is based on the phenomenologic aspects of the reaction and does not concern psychopharmacologic evaluations. Three groups, *A*, *B* and *C*, based on responsivity to the drug were established. Group A comprises patients who show striking changes in the disclosed thought content, as well as in general attitude. These patients revealed thought material previously unknown and assumed attitudes which were in contrast to those observed prior to the injection of sodium amytal. In group B were placed patients whose reactions differed from their usual behavior pattern through more willingness to communicate and change in emotional tone, whereas the expressed thought contents remained essentially uninfluenced. Group C consisted of patients who did not manifest psychologic changes. The content of thought and the emotional behavior pattern remained uninfluenced. The same technic of administering sodium amytal was used with all patients. The injection was given while the patient lay relaxed on a bed. The dose varied from 5 to 15 grains (0.975 to 0.325 Gm.), given as a 5 to 10 per cent solution. Each interview was started with the beginning of the injection, and the needle was held in the vein until the patient had reached and maintained a satisfactory state of narcosis.

Case Material.—The diagnostic classification of the 56 patients, taken from the hospital records, is as follows:

1. Schizophrenic, 31 patients; paranoid, 14; catatonic, 13; hebephrenic, 2, and simple, 2.

2. Affective disorder, 14 patients: manic type, 3; depressive, 6; involutional, 5.

3. Organic psychosis, 3 patients; dementia paralytica, 2; epilepsy with clouded states, 1.

4. Personality disorders without psychosis, 8 patients: psychopathic personality, 2; alcoholism, 3; simple maladjustment, 2 and conversion hysteria, 1.

RESPONSE GROUPS

GROUP A.—Of the 18 patients in this group, 5 had affective disorders; 9, schizophrenia; 1, an organic psychosis, and 3, minor type of personality disorders.

The brevity of this report does not permit description of the patients' reactions; suffice it to say that remarkable changes were observed. One catatonic patient, who had been mute and akinetic, danced, talked and even imitated himself. Another catatonic patient, also mute and rigid, stated during the interview: "It is not proper for me to talk; I have no power to change my posture; the injection broke the tissues down and made me able to talk to you." A man in a depressed stupor became agitated and experienced the torture of seeing his wife having intercourse with hundreds of sailors.

GROUP B.—Of the 16 patients in this group, some showed greater willingness to talk; others displayed a friendlier and more emotionally accessible attitude, but none of them disclosed any new thought content. These patients included 3 with affective disorders; 1 with a manic and 2 with a depressive psychosis; 8 with schizophrenic disorders, including 4 with the paranoid, 2 with the catatonic, 1 with the simple and 1 with the hebephrenic type; 1 with an organic disorder, dementia paralytica, and 4 with minor disorders, 2 being maladjusted, 1 psychopathic and 1 alcoholic.

A manic patient, for instance, who talked incessantly but had been rather hostile and aggressive toward the physician, became friendly and flirtatious under the influence of the injection, but continued to talk in her usual fashion. Depressed patients showed an increased ability to keep up conversation; paranoid patients were more accessible and showed less hostility and agitation, but expressed their usual delusions.

GROUP C.—This group consisted of 22 patients. Their psychologic reactions lacked significant change, as they remained uninfluenced in their attitude and in the expressed thought contents. The group included 6 patients with affective disorders, 1 of whom had a manic and 5 a depressed psychosis; 14 with schizophrenic disorders, 6 of whom had the paranoid, 6 the catatonic, 1 the simple and 1 the hebephrenic type; 1 with an organic disorder, epilepsy with a paranoid tendency and clouded states, and 1 with a minor disorder, alcoholism.

COMMENT

Analysis of the phenomenologic aspects of these data indicates, first, the absence of correlations between diagnostic categories and types of responsivity; all types of mental disorders are represented in each of the three groups. Comparison of the groups in regard to the number of patients reveals 18 in group A, 16 in group B and 22 in group C.

This means that only a relatively small part manifested a significantly changed attitude, while the greater part showed only moderate changes or were not influenced by the treatment. This observation is intesesting in view of the fact that the phenomenon of "lack of change" has been somewhat neglected in the literature on the method. Many investigators have evaluated selected responses, which were perhaps characteristic of certain mental disturbances, and have generalized their interpretations in conformity with dynamic preconceptions. A critical appraisal of the diversity of reactions does not support the frequently expressed opinion that the deeper levels of the personality begin to speak according to the depth of narcosis and that repressed and unconscious material comes freely to the surface. This claim is based on the belief that the unconscious system represents a regular level or space within the personality structure, a hypothesis which, as must not be forgotten, is not to account for neurotic symptoms only, but to have universal validity and to throw light on normal and abnormal mental functioning. It is difficult to understand how conceptions of unconscious forces within the personality can be so spatial, so architectural in nature as to permit the establishment of an equation according to which depths of narcosis correspond to certain levels of personality. To understand the significance of the diversity of responses, one must maintain the perspective of a total personality. An altered state of consciousness as induced by the drug can represent neither personality levels nor a realm of autonomous dynamisms. The assumption that repression is a prerequisite of symptom formation finds little support in the data of this study. Removal of inhibitory influences failed to change the phenomenologic aspects of symptoms of 22 patients in group C and of 16 in group B, who, whatever changes they showed, did not reveal thought contents which could be traced to sources of which the patient was not conscious. Of the 18 patients in group A who did manifest striking changes, some revealed material which had been consciously subjugated, and others expressed inner experiences which were not within the sphere of consciousness.

A qualitative evaluation of the various types of response enables one to discern and to understand in what manner the symptoms depend on totally altered personality function and to what extent they are influenced by subjective experiences. This will be more clearly understood as one examines some of the responses. One of the mute catatonic patients, for instance, disclosed during the interview that he did not talk because voices would creep into his mouth and emerge through his ears. Another catatonic patient stated he had to maintain one posture and could not talk because it would be "improper" for him to do so. Both cases show how the symptom of muteness and postural stereotypy is determined by certain inner experiences. These determinants are

secondary and can be understood only through recognition of the fundamental disturbance, which affects the person's entire orientation. The actual determinants of muteness and motor passivity in these 2 patients, however, were psychologic. These findings may be contrasted with observations on patients in depressed stupor who failed to manifest changes under the influence of the drug. They, too, showed muteness and motor passivity. Here, however, the symptoms seemed to be caused by a fundamental retardation in personality function, which affected motor, intellectual and emotional activities alike. If intentionality is totally impaired or altered, clouding of consciousness does not affect the phenomenologic nature of symptoms. The clinical importance of the recognition of primary and secondary determinants can be demonstrated in the case of a patient with neurosyphilis. This good-looking, middle-aged woman responded well serologically but became increasingly preoccupied and negativistic. She shaded her eyes with her hands while walking around and ignored her environment completely. While under the sodium amytal narcosis, she talked with a friendly and soft voice; she indicated that she could not pay any attention to her environment, as she had to concentrate all her attention on listening to the voice of her husband. (The patient's husband had left her after he learned the nature of her illness.) She denied emphatically that she worried about her husband's attitude, saying that he was hers as long as she could hear him talking to her. The narcodiagnostic method in this case revealed that certain symptoms of her psychosis were caused by inner experiences which enabled her to remain close to her husband. These symptoms of her psychosis could not be attributed simply to the fundamental, in this case organic, factor, but were determined by secondary formations, which represented her way of adjusting to the marital situation.

It is outside the scope of this investigation to examine the complex nosologic and etiologic aspects of primary and secondary determinants. Claude oversimplified the interpretation of his etherization method, for he declared determinants to be either psychogenic or organic. The briefly outlined evaluation of observations in this investigation shows that a phenomenologic analysis of fundamental and secondary factors can contribute to one's knowledge of determinants and symptom formation. One seems justified, therefore, in concluding that the narcotic method has potentialities as an instrument for psychopathologic investigations.

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POSTOPERATIVE PERIOD OF SURVIVAL OF PATIENTS WITH OLIGODENDROGLIOMA OF THE BRAIN

Report of Twenty-Five Cases

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OF THE intracranial gliomas, the group described as the oligodendrogliomas has been considered relatively benign. Since these tumors infiltrate the surrounding brain, complete removal may be impossible; yet recurrent symptoms have been reported only after a lapse of three to five years. Recently, however, this point has been questioned.[1] In an attempt to throw further light on the matter, we have reviewed the clinical course in 25 cases of verified oligodendrogliomas in the files of the neurosurgical laboratory of the Hospital of the University of Pennsylvania.

PRESENT INVESTIGATION

In 6 of the 25 cases in this series (24 per cent) the tumor was intraventricular, presumably arising from the walls of the ventricle. In 2 cases the tumor lay wholly within one of the lateral ventricles—in 1 case in the right and in the other in the left. The third ventricle appeared to be the original site of growth in 4 cases, the tumor spreading through the foramens of Monro into both lateral ventricles in 2 cases and into the right lateral ventricle only in the other 2 cases. These tumors were all solid growths, 3 of which were visualized before operation because of calcification within the tumor. No basis for histologic differentiation of this type of oligodendroglioma could be deduced.

In the remaining 19 cases the tumor was classified as the intrahemispheric type. In 4 of these cases the tumor, while growing chiefly in the substance of the cerebrum, extended nevertheless into the lateral

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From the Departments of Neurosurgery and Neuropathology of the Hospital of the University of Pennsylvania.

1. (*a*) Eisenhardt, L.: Long Postoperative Survivals in Cases of Intracranial Tumor, A. Research Nerv. & Ment. Dis., Proc. (1935) **16**:390-416, 1937. (*b*) Elvidge A.; Penfield, W., and Cone, W.: The Gliomas of the Central Nervous System, ibid. **16**:107-181, 1938.

ventricles. It is interesting to note that in 4 other cases of this group the tumor, when first visualized at operation, appeared to be extracerebral and was thought to be a meningioma. However, when the discrete surface of the tumor was dissected free, it was noted that the base of the growth arose from the brain substance, and only at this point did its gliomatous nature become clear. Oligodendrogliomas of this type, again, showed no histologic differentiation from the more obviously infiltrating type. The appearance was generally described as soft, reddish and vascular. Occasionally it was noted that the tumor was, in addition, granular and friable. In several instances the surrounding white matter was unusually hard, and histologic sections of this area showed considerable reactive gliosis of the parenchyma about the tumor. In almost all instances in which sufficient material was available the zone of growth of the tumor was extremely narrow.

In 8 of the cases of the intrahemispheric type the tumor was located in the right frontal area, and in 4, in the left frontal area. In 4 cases the growth occurred in both frontal areas, being predominantly in one or the other hemisphere in 3 cases and being equally distributed in the two frontal lobes in 1 case. In 3 cases the tumor was located in the left parietal lobe. These data emphasize the predominant frontal localization of the oligodendrogliomas.

In 13 of the 25 cases the tumor was sufficiently calcified to be recognized in the preoperative roentgenogram. In 5 other cases calcification was described in the histologic preparation only. The calcification was noted to be related primarily to the blood vessels.

None of the tumors of the ventricular type was cystic, but 5 of the remaining 19 oligodendrogliomas in this series contained definite cystic areas. In no instance was cyst formation predominant throughout the tumor. In 1 instance the cysts were recognized only microscopically.

Histologically, the tumors revealed the characteristics described by Bailey and Cushing [2] and amply confirmed by later authors.

Clinical Features.—Tumors of the ventricular type occurred at a significantly earlier age than did those of the hemispheric type. The ages of the patients with the ventricular type averaged 25 years, with a range of 19 to 29 years. The ages of the patients with the hemispheric type averaged 37 years, with a range of 21 to 58 years. The series was almost equally divided as to sex, with 12 women and 13 men.

In the 6 cases of ventricular tumor the average preoperative period was seven and two-thirds months, with a range of three to eleven months. The early symptoms were those of increased intracranial pressure. Focal signs were generally absent, or, if present, appeared late in the course

2. Bailey, P., and Cushing, H.: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

of the disease. Convulsive seizures did not occur before operation in this group, although in 2 of the 6 cases there occurred attacks of decerebrate rigidity, caused by recurrent crises of increased intracranial pressure.

The preoperative duration of symptoms in the 19 cases of intrahemispheric tumor averaged thirty-five months, with a range of five to one hundred and four months. The onset of symptoms in 9 cases was with focal neurologic signs and epileptic seizures. The latter were of jacksonian nature in 7 cases and were generalized in 2 cases. In 6 of these 9 cases symptoms of increased intracranial pressure later developed. The initial symptoms in the 10 remaining cases were those of increased intracranial pressure. In 9 of these 10 cases focal symptoms and signs of the cerebral lesion appeared later in the course of the disease and in 3 cases epileptic seizures occurred.

It is thus evident that in 12 of the 19 cases of intrahemispheric tumor epileptic seizures occurred prior to operation.

Course and Prognosis.—The average postoperative life span of 20 patients was twenty-one months. Of this group, 4 are still alive, ten to fifty months after operation. Five patients in our series (20 per cent) died in the immediate postoperative period.

Ventricular Group: One patient died on the first postoperative day. He had had symptoms of thirteen months' duration, the predominant feature of which in the last few months of his life was repeated episodes of decerebrate rigidity. The tumor was located in the third ventricle and had extended into each of the lateral ventricles.

One patient is still alive, fifty months after her first operation. She had a recurrence of symptoms of increased intracranial pressure requiring a second operation seven months after the initial procedure. The tumor, located in the left lateral ventricle, was thought to have been completely removed at the second operation. She is now asymptomatic, does all her own housework and is successfully raising a family. She was not given radiation therapy at any time.

The 4 remaining patients with ventricular tumors had survival periods of two, three, twenty-two and twenty-three months, respectively, with an average of twelve and one-half months. One of these patients had three courses of intensive radiation therapy, without apparent effect on the course of the disease. None of these patients had epileptic seizures after operation, and all died of recurring symptoms of increased intracranial pressure.

Intrahemispheric Type: There were 4 postoperative deaths in the series of patients with oligodendroglioma infiltrating the cerebrum. Four patients are still alive, thirty, fifteen, ten and ten months after operation. None of the latter is fully capable. Two are physically well but mentally incapable of holding a job and, in addition, have occasional epileptic

seizures, although these are generally well controlled with medication. One patient has a residual hemiplegia and exhibits serious personality changes. The last of this group, who still survives, is mentally intact and has no residual neurologic disturbances other than total blindness, which was present before operation and was due to severe papilledema. The remaining 11 patients survived an average of twenty-two months, the periods ranging from five to forty-eight months. However, the patients whose tumor extended outside the cortex had a distinctly longer period of survival (thirty-two months) than the patients whose tumor was limited to the brain substance (eighteen and one-half months).

Four patients in this group had a second operation for recurrence of symptoms anywhere from one to two years after the original procedure. All died within six to eight months after the second exploration. Two of this group died of intercurrent disease, without evidence of recurrence of symptoms of the cerebral tumor. One died of carcinoma of the pancreas sixteen months after operation, and 1, of acute ascending myelitis (verified at autopsy) forty-five months after operation. Histologic examination of the brain at necropsy did not reveal recurrence of the cerebral tumor. Nine of these 11 patients had convulsive seizures after operation; 2 died in status epilepticus—1, eight and 1 nineteen months after operation. Abrupt cessation of anticonvulsant therapy was the immediate cause of the status epilepticus.

COMMENT

The predisposition of oligodendrogliomas to grow within the ventricle was remarked on by Greenfield and Robertson.[3] A few years later, Löwenburg and Waggoner [4] emphasized this point and reported that the growth of the oligodendroglioma in 2 cases, in a series of 21, was largely confined to the ventricles. Of our entire series, the oligodendroglioma could be classified as the ventricular type in 24 per cent. Our observations further confirmed the experience of Löwenburg and Waggoner,[4] namely, that the frontal lobes are the favored site of growth of this type of glioma and that there is a distinct tendency of the growth to spread from one hemisphere to the other across the midline, through the corpus callosum.

From the results of this study, we were unable to confirm recent reports [5] that there is a tendency of oligodendrogliomas to disseminate

3. Greenfield, J. G., and Robertson, E. G.: Cystic Oligodendrogliomas of the Cerebral Hemispheres and Ventricular Oligodendrogliomas, Brain **56**:247-264, 1933.

4. Löwenburg, K., and Waggoner, R. W.: Gross Pathology of the Oligodendrogliomas, Arch. Neurol. & Psychiat. **42**:842-861 (Nov.) 1939.

5. Löwenburg and Waggoner.[4] Beck, D. J. K., and Russell, D. S.: Oligodendrogliomatosis of the Cerebrospinal Pathway, Brain **65**:352-372, 1942. Blumenfeld, C. M., and Gardner, W. J.: Disseminated Oligodendroglioma, Arch. Neurol. & Psychiat. **54**:274-279 (Oct.) 1945.

through the meninges of the cerebrospinal axis. Failure to observe such a tendency could well be due to the few autopsy records available in this series. At operation, in several instances, seeding on the ependyma of the ventricle, at a distance from the main mass of the lesion, was noted.

Bailey and Cushing,[2] when first reporting on this type of glioma, remarked on the long course of the tumors and gave the postoperative survival as four plus years. Bailey and Bucy,[6] in 1929, reported that the average postoperative period of survival in a series of 13 cases of oligodendroglioma was 39.2 months, with an average preoperative duration of symptoms of 57.5 months. The ultimate outcomes in series of tumors of the brain observed by Van Wagenen,[7] Cairns [8] and Davidoff,[9] during their services with Dr. Cushing, were reported in 1934, 1936 and 1940, respectively. Data on the small series of cases of oligodendroglioma followed by these observers generally confirmed the favorable prognosis previously noted for this type of glioma. Elvidge, Penfield and Cone [1b] were the first to note that postoperative survival in cases of oligodendroglioma was disproportionately lower than the preoperative duration. In their series of 8 cases, the preoperative duration of symptoms averaged 11.7 years, with postoperative survival periods of three, three, two and one-half, and one-third years—3 of the patients in their series being still alive four, eleven and sixteen months after operation. They stated the belief that the rate of growth of this type of glioma tends to increase late in its evolution and that operation speeds it up yet more. While this discrepancy between the preoperative and the postoperative duration is not so broad in our series, it is present. The average postoperative period of survival, indeed, was less than two years. The segregation of cases in which the tumor was growing particularly within the ventricular system altered the prognosis only slightly. It did appear that the preoperative duration of symptoms of patients with the ventricular type was shorter than that of patients with the hemispheric type, while there was little difference between the two groups in length of postoperative survival.

In no instance were there sufficient mitoses or other evidences of rapid growth which could be correlated with the clinical course of the patient to justify the formation of a group of cases of the oligoblastomatous type. It was not possible, therefore, from the histologic appearance

6. Bailey, P., and Bucy, P. C.: Oligodendrogliomas of the Brain, J. Path. & Bact. **32**:735-751, 1929.

7. Van Wagenen, W. P.: Verified Brain Tumors (End Results of One Hundred and Forty-Nine Cases Eight Years Postoperative), J. A. M. A. **102**:1454-1458 (May 5) 1934.

8. Cairns, H.: Ultimate Results of Operations for Intracranial Tumors, Yale J. Biol. & Med. **8**:421-492, 1936.

9. Davidoff, L. M.: A Thirteen Year Follow-Up Study of a Series of Cases of Verified Tumors of the Brain, Arch. Neurol. & Psychiat. **44**:1246-1261 (Dec.) 1940.

of the tumor, to segregate a group in which the prognosis could be said to be more favorable.

The symptomatology of this type of glioma is interesting, since there was a clear distinction between cases of the ventricular and cases of the hemispheric type. The former were characterized early by the symptoms of increased intracranial pressure. Focal signs and convulsive seizures were generally absent, or appeared late in the course of the disease. Focal convulsive seizures were common in cases of the hemispheric type, and often were the first manifestation of the disease. Penfield and Erickson [10] noted that the two factors which influence the relationship between brain tumor and epileptic seizures are the distance which separates the tumor from the sensorimotor cortex and the rapidity of growth of the tumor. The ventricular tumors are deep-lying lesions and make themselves manifest relatively quickly. The hemispheric lesions, usually superficial and generally located in the frontal lobes, are thus frequently associated with epileptic seizures.

SUMMARY

Six of the present series of 25 oligodendrogliomas (24 per cent) were located principally within a lateral and/or the third ventricle. Seventeen of the 19 oligodendrogliomas growing in the parenchyma of the brain were located in one or the other, or in both frontal lobes.

Patients with ventricular tumors had a short preoperative course (average of seven and one-half months), and the symptoms were those of increased intracranial pressure. Patients with hemispheric tumors had a longer preoperative duration of symptoms (average, thirty-five months), and the history generally was one of focal symptoms, often jacksonian seizures, preceding the symptoms and signs of increased intracranial pressure.

The average period of survival after operation in this series was less than two years. Of the 5 patients with ventricular tumor who survived operation, only 1 is still alive and well (at the end of fifty months). The average period of survival of the remaining 4 patients was twelve and one-half months, with a range of two to twenty-three months. Fifteen patients with hemispheric tumor recovered from operation, but only 4 are still alive, ten to thirty months later. The remaining members of this group survived an average of twenty-two months, with a range varying from five to forty-eight months.

3400 Spruce Street.

10. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

SIGNIFICANCE OF CHANGES IN THE ELECTROCARDIOGRAM AFTER ELECTRICALLY INDUCED CONVULSIONS IN MAN

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BELLET and associates [1] studied the effects of electrically induced convulsions on the electrocardiogram in man and recorded the frequent occurrence of sinoauricular block, sinus arrhythmia, shifting pacemaker, auricular premature beats and auriculoventricular nodal rhythm; these arrhythmias were considered to be consequent to vagal hyperactivity. Reference may also be found in the clinical literature to the occurrence of auricular fibrillation after electroshock therapy.[2] On the other hand, Nyman and Silfverskiöld [3] emphasized changes in the P and T waves and laid little emphasis on the development of arrhythmias and bradycardia. In order to evaluate the frequency, degree and significance of cardiac inhibition which might occur as a consequence of electrically induced convulsions, it was considered of interest to make further observations on the electrocardiogram and simultaneously to study the changes in the circulation time.

MATERIAL AND METHODS

Thirty studies were made in 10 patients. The ages of the subjects varied from 17 to 56; 9 were women. Five patients were studied once or twice, and the other 5 were studied four to seven times each.

From the Clinical Services of the McLean Hospital, Belmont; the Medical Research Laboratories of the Beth Israel Hospital, Boston, and the Departments of Psychiatry and Medicine of Harvard Medical School.

1. Bellet, S.; Kershbaum, A., and Furst, W.: The Electrocardiogram During Electric Shock Treatment of Mental Disorders, Am. J. M. Sc. **201**:167, 1941.

2. Hayman, M.: The Prophylaxis of Cardiac Complication in Electroshock Therapy, Am. J. Psychiat. **102**:316, 1945. Smith, L. H.; Hastings, D. W., and Hughes, J.: Immediate and Follow-Up Results of Electroshock Therapy, ibid. **100**:351, 1943.

3. Nyman, E., and Silfverskiöld, B. P.: Kreislaufstörungen bei Krampfanfällen epileptischen Typs: III. Das Elecktrokardiogramm beim Elektroschock, Acta med. Scandinav. **114**:223, 1943.

Standard three lead electrocardiograms were made before induction of the convulsive seizure. The electrocardiographic electrodes were left in place, and as soon as the convulsion was over another tracing from all three standard leads was begun. The circulation time was studied by the fluorescein method,[4] measurements being made before and again approximately one minute after the convulsion.

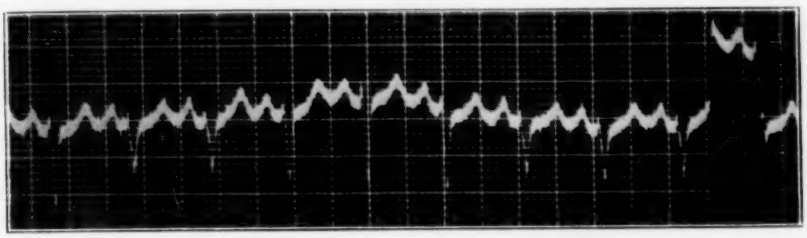

Fig. 1.—Rhythmic variation in QRS complexes with respiration after a convulsion.

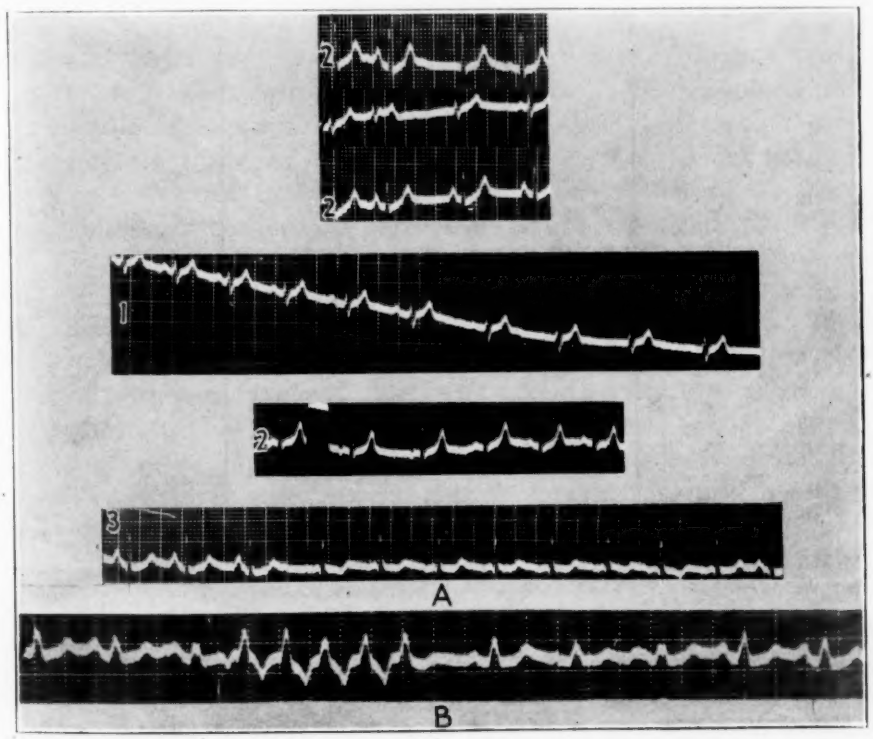

Fig. 2.—*A*, arrhythmias occurring on different occasions in the same patient after convulsion: sinus arrhythmia, auriculoventricular nodal rhythm, auricular premature beats and variations in the P-R interval. *B*, brief paroxysm of auricular tachycardia after convulsion.

4. Fishback, D. B.; Guttman, S. A., and Bramson, E. B.: An Objective Method of Determining Blood Velocity (Fluorescein Method), Am. J. M. Sc. **203**:535, 1942.

OBSERVATIONS

The average cardiac rate was accelerated in every instance. The increase in rate ranged from 22 to 94 per cent; the lesser increases occurred in patients in whom short but recurrent periods of arrhythmia developed. The ventricular gradient was decreased in 3 patients on whose tracings measurements were made.

Increase in the size of the P wave was a uniform finding at some time after the convulsion except when aberrant auricular or nodal beats occurred. Similarly, every tracing taken after the seizure showed a rhythmic variation in the size and shape of the QRS waves, the varia-

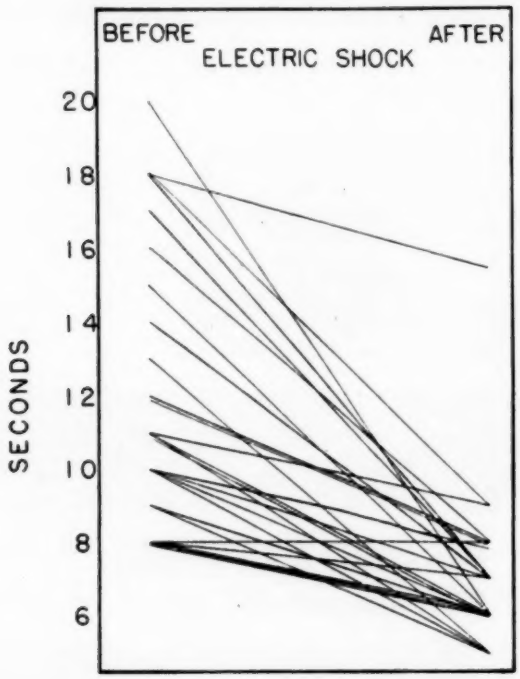

Fig. 3.—Circulation times before and after convulsion.

tion consisting in a change from tall, narrow complexes to short complexes and back again (figs. 1 and 3); the rhythm of this change corresponded with the respirations. Four patients studied a total of thirteen times showed depression of the S-T interval in one or more leads on eleven occasions (fig. 2 *A* and *B*); this was only minimal for 3 of the patients.

Arrhythmias occurred in all but 2 of the 10 patients. The patients who were studied four to seven times each did not necessarily exhibit arrhythmia on each occasion. It was found in all 4 studies on 1 patient, but in 3 others studied four or more times each it was found in only one-half the studies on each. The arrhythmias found most often were

a shifting pacemaker, auricular premature beats, pronounced sinus arrhythmia, periodic bradycardia and nodal rhythm (fig. 2 *A*); in addition, auricular tachycardia occurred in 1 instance (fig. 2 *B*). The arrhythmias changed from one type to another rapidly (fig. 2 *A* and *B*). One patient in whom a cardiac arrhythmia developed after the electrically induced convulsion exhibited occasional ventricular premature beats.

Studies of the circulation time showed acceleration of the blood flow after the convulsive seizure in every case (fig. 3).

COMMENT

The present study corroborates the previously recorded occurrence [1] after electrically induced convulsions of shifting of the site of origin of the heart beat, as evidenced by pronounced sinus arrhythmia, periods of sinus bradycardia, frequent auricular and nodal premature beats and, in 1 instance, auricular tachycardia. This type of disturbance in cardiac rhythm is a consequence of vagal hyperactivity; the results of a few studies by Bellet and associates [1] in which atropine minimized these changes are in accord with this concept. Similarly, the development of auricular fibrillation [2] after electroshock therapy is to be interpreted as a manifestation of increased vagal tone.[5] The occurrence of vagal arrhythmia goes with other evidences of autonomic stimulation exhibited by patients during and after convulsive seizures. It is not clear, however, whether the increase in vagal tone in the heart is the result of stimuli from the brain, of reflexes activated by the cardiorespiratory changes induced by the convulsion [6] or of the potentiation of acetylcholine action by the acidosis which occurs [6a] as a result of high carbon dioxide levels. Similarly, the part played by asphyxia [6a] in the genesis of the vagal stimulation observed cannot be evaluated. However, irrespective of the mechanism of production of increased vagal tone during electrically induced convulsions, it is probable that the acidosis which occurs [6a] as the result of accumulation of carbon dioxide increases the action of whatever acetylcholine is liberated by inhibiting cholinesterase and thereby potentiating the vagal inhibition of the heart.[7] The vagal hyperactivity noted does not give rise to sufficient cardiac inhibition

5. Altschule, M. D.: Relation Between Vagal Activity and Auricular Fibrillation in Various Clinical Conditions, New England J. Med. **233**:265, 1945.

6. (*a*) Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Effects of Electrically Induced Convulsions upon Respiration in Man, Am. J. Psychiat **103**:680, 1947. (*b*) Silfverskiöld, B. P., and Åmark, C.: Disturbance of Circulation in Convulsions of the Epileptic Type: II. Arterial and Venous Pressures During Electroshock, Acta med. Scandinav. **113**:191, 1943. (*c*) Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Effect of Electrically Induced Convulsions on Peripheral Venous Pressure in Man, Arch. Neurol. & Psychiat. **58**:193 (Aug.) 1947.

7. Gesell, R.; Mason, A., and Brassfield, C. E.: Acid Humoral Control of Heart Beat, Am. J. Physiol. **141**:312, 1944.

to slow the systemic circulation and is therefore not a factor in the increase in venous pressure which occurs during electrically induced convulsions.[8] It appears that the occurrence of this type of arrhythmia usually gives rise to no hazard in patients without antecedent cardiac disease. It is to be noted that arrhythmias of vagal origin may also occur after seizures induced with convulsant drugs.[9]

The increase in the size of the P wave which occurred during the immediate postconvulsive period is of some interest in that it probably is an indication of dilatation of the auricle, consequent here to increased venous pressure and venous return. Earlier studies[8] revealed the development of high venous pressure levels during electrically induced seizures and evidence of increased venous return immediately after the seizure. It is of interest that a similar increase in size of the P wave has been noted in patients receiving large infusions intravenously,[10] and after the Valsalva procedure,[11] and is also well known to occur with auricular dilatation consequent to mitral stenosis.

Changes in the ventricular complexes caused by convulsions are not important. The rhythmic variation in the shape of the QRS complex observed in all cases is probably respiratory in origin; respiration for several minutes after the seizure is markedly hyperpneic[6a] and shifts in the level of the diaphragm must be extreme. The variable changes in the T waves and the inconstant depression of the S-T interval noted were not significant, for they were not associated with changes in the direction of the ventricular gradient.

SUMMARY

The electrocardiogram after electrically induced convulsive seizures often shows evidence of a considerable increase in tone of the vagus innervation of the heart. The increase in vagal activity usually does not induce sufficient cardiac inhibition to cause more than transitory bradycardia; the systemic circulation is not slowed. Other electrocardiographic changes associated with variations in respiration and circulation after electroshock therapy are also noted.

McLean Hospital.

8. Silfverskiöld and Åmark.[6b] Altschule, Sulzbach and Tillotson.[6c]

9. Dick, A., and MacAdam, W.: Cardiac Complications in Cardiazol Treatment: Observations in Four Cases, J. Ment. Sc. **84**:677, 1938.

10. Altschule, M. D., and Gilligan, D. R.: Effects on the Cardiovascular System of Fluids Administered Intravenously in Man: II. The Dynamics of the Circulation, J. Clin. Investigation **17**:401, 1938.

11. Liedholm, K.: Studien über das Verhalten des Venendrucks beim Valsalvaschen Versuch, Acta med. Scandinav., 1939, supp. 106.

SPATIAL ORGANIZATION OF VISUAL PERCEPTION FOLLOWING INJURY TO THE BRAIN

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IN A SYSTEMATIC study of patients who had sustained battle injuries of the parieto-occipital lobes,[1] we found 12 with spatial disorientation. The disorders ranged in severity from almost complete "space blindness" to conditions in which the defect seemed confined to homonymous halves, quadrants or even sectors of the fields of vision. Particularly the patients with sector defects presented highly consistent symptoms. However, none of the findings could readily be explained in terms of current theories of visual space perception. Before embarking on an analysis of our case material, we shall, therefore, trace some of the previous attempts at a neurologic and psychologic interpretation of disorders in the visual perception of spatial relations.

Prior to World War I, a disorder in the perception of spatial relations was considered part of a generalized disturbance in intellectual function. Loss of orientation in space as well as the inability to localize objects in space were thus described as more or less incidental symptoms in cases of post-traumatic confusional states and of severe visual agnosias.[2] Moreover, the clinician's description of the symptoms was

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as official or reflecting the policies of the Navy Department.

1. (*a*) Bender, M. B., and Teuber, H. L.: Fluctuation, Extinction and Completion in Visual Perception, Arch. Neurol. & Psychiat. **55**:627 (June) 1946; (*b*) Ring Scotoma and Tubular Fields: Their Significance in Head Injury, ibid. **56**:300 (Sept.) 1946.

2. (*a*) Jackson, J. H.: Case of Cerebral Tumour Without Optic Neuritis and With Left Hemiplegia and Imperception, Roy. London Ophth. Hosp. Rep. **8**:434, 1876. (*b*) Hartmann, F.: Die Orientierung, Leipzig, F. C. W. Vogel, 1902. (*c*) Balint, R.: Seelenlähmung des Schauens, optische Ataxie, räumliche Störung der Aufmerksamkeit, Monatschr. f. Psychiat. u. Neurol. **25**:51, 1909. (*d*) von Stauffenberg, W.: Ueber Seelenblindheit: Nebst Bemerkungen zur Anatomie der Sehstrahlung, Arb. a. d. hirnanat. Inst. Zürich **8**:1, 1914.

often vitiated by an uncritical acceptance of the available psychologic theories of space perception.

Von Stauffenberg's approach [2d] may be considered characteristic of this attitude. A "visuospatial agnosia" was assumed to involve a peculiar difficulty in the invoking of "visuomotor engrams." The latter, in turn, was thought to be due to the fact that the patient's momentary visual impressions had become too indistinct to allow him to elaborate or mobilize the requisite "spatial signs." Such an analysis implicitly accepted a host of psychologic concepts and theories (e. g., "engrams," "mnemic dispositions") which were current at the time, before the first world war.[3] On the whole, the problem was not critically attacked until pathologic material became abundant. During and after the first world war there were many cases of changes in perceptual functions as the result of gunshot wounds of the brain. Among these were the classic instances of disorders in the visual perception of space—the cases described by Holmes,[4] Riddoch,[5] Goldstein and Gelb,[6] Fuchs,[7] Poppelreuter,[8] Best,[9] Piéron [10] and many others. (For summaries of these cases, see Kleist [11] and Klüver.[12])

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3. It is noteworthy that, as late as 1941, W. R. Brain (Visual Object-Agnosia with Special Reference to the Gestalt Theory, Brain **64**:63, 1941) analyzed a case of "mind-blindness" basically in the same terms as did von Stauffenberg,[2d] in 1914.

4. Holmes, G.: (*a*) Disturbances of Visual Orientation, Brit. J. Ophth. **2**: 449 and 506, 1918; (*b*) Disturbances of Visual Space Perception, Brit. M. J. **2**: 230, 1919.

5. Riddoch, G.: Dissociation of Visual Perception Due to Occipital Injuries, with Especial Reference to Appreciation of Movement, Brain **40**:15, 1917.

6. (*a*) Goldstein, K., and Gelb, A.: Zur Psychologie des optischen Wahrnehmungs und Erkennungsvorgangs, Ztschr. f. d. ges. Neurol. u. Psychiat. **41**:1, 1918. (*b*) Gelb, A., and Goldstein, K.: Psychologische Analysen hirnpathologischer Fälle auf Grund von Untersuchungen Hirnverletzer, Leipzig, Johann Ambrosius Barth, 1920. (*c*) Gelb, A.: Die psychologische Bedeutung pathologischer Störungen der Raumwahrnehmung, Ber. ü. d. Kong. f. exper. Psychol. **9**:22, 1926.

7. Fuchs, W.: Untersuchungen über das Sehen der Hemianopiker und der Hemiamblyopiker, Ztschr. f. Psychol. **86**:1, 1921.

8. (*a*) Poppelreuter, W.: Die psychischen Schädigungen durch Kopfschuss im Kriege 1914-1916: I. Die Störungen der niederen und höheren Sehleistungen durch Verletzungen des Okzipitalhirns, Leipzig, Leopold Voss, 1917, vol. 1; (*b*) Zur Psychologie und Pathologie der optischen Wahrnehmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:26, 1923.

9. Best, F.: (*a*) Hemianopsie und Seelenblindheit bei Hirnverletzungen, Arch. f. Ophth. **93**:49, 1917; (*b*) Ueber Störungen der optischen Lokalisation bei Verletzungen und Herderkrankungen im Hinterhauptlappen, Neurol. Centralbl. **38**:427, 1919.

10. Piéron, H.: (*a*) Des degrés de l'hémianopsie corticale: l'hémiastéréopsie, Compt. rend. Soc. de biol. **74**:1955, 1916; (*b*) Thought and the Brain, New York, Harcourt Brace & Company, 1927.

The most obvious result of the work of these investigators was an increase in factual knowledge. Thus, some observers, such as Riddoch,[5] noted that certain forms of spatial disorientation could be limited to the visual sphere, and even to homonymous half-fields. Yet in the interpretation of their findings the majority of the authors, as represented by Holmes,[4] Riddoch,[5] Piéron [10a] and Best,[9b] continued to use the conceptual tools of the traditional theory of space perception.

These traditional theories of space perception, which still loom so large in neurologic terminology, are basically associationistic, although the "mental elements" of the older associationistic doctrines may have been cast into the form of reflexes and quasireflexes of the neopavlovian school.[13] The general assumption of these theories is as follows: Tridimensional organization of perception is always a complex process, based on the secondary integration, in "higher" cortical centers, of originally bidimensional and unnoticed sensations (the "cues" of distance and depth).

Localization in the bidimensional (coronal) plane itself is assumed to be based on a simple direction factor, viz., the specific "local sign" of each retinal point.[14] Tridimensional space, according to the same traditional theories, is achieved by the organism on the basis of even more complex processes of integration and interpretation of sensory data. Stereoscopic vision is thus "elaborated" from the famous cues of depth.[15]

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11. Kleist, K.: Kriegsverletzungen des Gehirns, in Handbuch der ärtzlichen Erfahrungen im Weltkriege, Leipzig, Johann Ambrosius Barth, 1922, vol. 4, p. 343.

12. Klüver, H.: Visual Disturbances After Cerebral Lesions, Psychol. Bull. **24**:316 and 358, 1927.

13. Lashley, K. S., and Wade, M.: The Pavlovian Theory of Generalization, Psychol. Rev. **53**:72, 1946.

14. On the basis of a concept of Lotze (Medicinische Psychologie, oder Physiologie der Seele, Leipzig, Weidmann, 1852), who formulated it in a somewhat different connection, local signs are considered to determine the above and the below, the right and the left, in the visual field with relation to the anatomic fovea.

15. These cues are usually classified as uniocular and binocular. Considerable effort has been spent in study of the former, since it has always been known that monocular subjects may possess excellent depth perception. Under normal conditions, however, the most essential determinant for any accurate perception of depth and distance is assumed to be furnished by binocular vision, or the so-called binocular parallax. This is the stereoscopic effect of the fusion of the slightly dissimilar images obtained by the two eyes. The traditional views on depth perceptive are well developed in Carr's monographic presentation (Carr, H.: An Introduction to Space Perception, New York, Longmans, Green & Company, 1935). Brief orientations were given by Woodworth [49] (pp. 651-683) and by Duke-Elder (Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 1, pp. 1038-1058 ["Binocular Perceptions"] and 1059-1081 ["Perception of Space"]). For a historical orientation, see Boring (Boring, E. G.: Sensation and Perception in the History of Experimental Psychology, New York, D. Appleton-Century Company, Inc., 1942, pp. xv and 644).

Under the influence of these assumptions concerning normal space perception, not only the analysis, but even purely clinical descriptions, of the pathologic material tended to become biased. Neurologists endeavored to identify the particular monocular or binocular "cues" that had become unavailable for the patient. Single factors, such as spasms of accommodation and disorders in oculomotor reflexes (Piéron [10a]), were suggested as "causes" of the subjective distortions of visual space. The possibility of a total loss of stereoscopic vision was quite seriously considered (Holmes [4b]). As in the numerous studies on aphasia, the organism was expected to lose its various functional capacities in accordance with the subdivisions of the textbooks.

However, before the end of the first world war, a new trend of research was inaugurated by Kurt Goldstein and his collaborator Adhémar Gelb.[6] They introduced the concepts of the gestalt theory, which was just then emerging from the psychologic laboratories.[16] However, they did not simply exchange one set of psychologic predilections for another. By challenging the traditional theories, they reopened the entire question of the physiologic basis of space perception. They insisted on a strictly empiric description of the behavioral changes in patients with cerebral lesions. By means of their analyses they developed two principal themes: 1. They described a general syndrome of altered space perception, characterized by "loss of abstract spatial relations." Patients with such a disturbance showed changes in more than one sensory sphere. However, they were not necessarily completely disoriented, since they could often fall back on a concrete motor sequence [6a] which enabled them to deal fairly efficiently with the spatial aspects of their surroundings. 2. They emphasized the influence of postural tone on perceptual organization, and vice versa.[17]

16. The work of the principal representatives of the gestalt "school" (Wertheimer, Köhler, Koffka, Goldstein and Gelb) has been excellently summarized by Hartmann (Hartmann, G. W.: Gestalt Psychology: A Survey of Facts and Principles, New York, Ronald Press Company, 1935, p. 325). Ellis (Ellis, W. D.: A Source Book of Gestalt Psychology, New York, Harcourt Brace & Company, Inc., 1938) translated abstracts of some of the German publications on the gestalt theory. According to the German writers, the gestalt concept can be described as "any configuration which in its total organization contains more functional properties than the sum of its apparent component parts." With regard to perception, the gestalt theory stresses that organisms react not to discrete stimuli but to total situations. The total situation includes not only the stimulus configuration but also an intrinsically organized pattern of reaction on the part of the responding organisms.[23]

17. (*a*) Goldstein, K., and Riese, W.: Ueber induzierte Veränderungen des Tonus, Klin. Wchnschr. **2**:1201, 1923. (*b*) Goldstein, K., and Jablonski, W.: Ueber den Einfluss des Tonus auf Refraktion und Sehleistungen, Arch. f. Ophth. **130**: 395, 1933. (*c*) A recent review of some of the relevant experimental data has been made by H. Werner (Motion and Motion Perception: A Study on Vicarious Functioning, J. Psychol. **19**:317, 1945).

This second point, however (the observations on a "tonic substrate of perception"), was somewhat lost sight of in the vigorous debates which followed their original publications. The focus of attention was on the total or partial loss of the patient's ability to manipulate abstract spatial relations. For a while, the clinical phenomena figured prominently in the discussions between the proponents of the older theories of perception and those of the emergent gestalt school. It was then fully recognized that the pathologic material offered clues to an understanding of the physiologic basis of visual perception—both normal and abnormal.

One of the primary concerns of the gestalt group in their opposition to the traditional theory was an effort to overcome the distinction of "simple" and "complex" processes in perceptual functioning. Tridimensional visual space, they asserted, is inherent in all processes of visual perception. The classic "cues" of depth and distance were admitted to be necessary conditions for an accurate judgment of depth and distance, but in themselves they were not considered sufficient to make depth perception possible.[18]

According to the gestalt theory, depth, distance and shape of visual percepts are conceived as determined by the distribution of forces within a hypothetic "field of forces." The visual field at any moment is organized into "figures" (*Gestalten*) on a "ground" (background). These figures are held together (and "in place," relative to the background) by intrinsic forces, which are assumed to be in stable equilibrium for "strong," or "good," *Gestalten* (such as a circle, seen in the coronal plane), and in unstable equilibrium for "weak," or irregular and ill defined, *Gestalten* (such as any asymmetric figure tilted out of the coronal plane). The assumption of these figure forces is an inference based on a variety of perceptual phenomena. Among these is the

18. In experiments with normal subjects and with subjects with injuries of the brain, the gestalt psychologists endeavored to show that the various "cues" are active only so far as they enter into the total stimulus situation. Thus, they investigated the formation of pseudofoveas in hemianoptic patients in order to demonstrate that the retinal "local signs" must be functional, and cannot be based on structural, point for point relationships. In effect, they added certain factors in depth perception which had received little, or no, attention in the classic doctrine. They emphasized the inherent depth effects of certain colors which may become enhanced after cerebral trauma (Gelb, A., and Goldstein, K.: Ueber den Wegfall von "Oberflächenfarben," Ztschr. f. Psychol. **84**:193, 1920), and they added the factor of a binocular time parallax to supplement the long-recognized role of spatial binocular disparity in the depth localization of objects which move rapidly past the eyes (Klemm, O.: Die binokulare Zeitparallaxe, Neue Psychol. Stud. **6**: 357, 1932). H. Werner (Dynamics in Binocular Depth Perception, Psychol. Monogr. **49**:1, 1937) has begun to develop a unitary theory of monocular and binocular depth perception in which the physiologic processes underlying the stereoscopic effect are brought into close relation with so-called stroboscopic effects.

tendency toward "closure"; a good *Gestalt*, e. g. a circle, is readily seen as complete and closed, even though it may have a gap.[19]

Such hypothetic field forces or "vectors," have shown their heuristic value in the consideration of specific problems of normal perception. They were found to be useful conceptual tools in analyzing the apparent distortion of lines (in the so-called optical illusions [20]) and in predicting the path of apparent movement.[21]

In all these instances, the "vectors" are derived from an analysis of the stimulus distribution within the visual field (e. g., in the instance of optical illusions, the particular line patterns which surround the apparently distorted test figure). However, the implicit assumption is that the visual apparatus, notably the striate cortex itself, reacts as a "field" to photic stimulation. Köhler, in particular, endeavored to demonstrate the existence of such a "cortical field," in which the inferred vectors are represented by actual changes in the electrotonus during and after the acts of perception (Köhler and Wallach [22]). The hypothesis undoubtedly helps to clarify a number of obscure phenomena of normal vision.

On the other hand, the introduction of these concepts of fields of force has been justly criticized because they involve a number of *ad hoc* assumptions (Goldstein [23]) and because they are exceedingly difficult to cast into concrete neural terms.[24] Evidently, the older associationistic or quasiassociationistic theories have the advantage of agreeing well with the predominant conception of the central nervous system as an aggregate of synaptic junctions.

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19. Thus, as Koffka (Koffka, K.: Some Problems of Space Perception, in Murchison, C.: Psychologies of 1930, Worcester, Mass., Clark University Press, 1931) has pointed out, a perspective drawing of a cube will be seen in three dimensions, not because of any binocular cues (it can be viewed monocularly, and still gives the impression of depth), or because of experience (or assimilation with stored images of cubes), since actual cubes look very different indeed from a schematic perspective drawing. Koffka's explanation is, rather, that the line pattern becomes a "better" (more equilibrated, more symmetric) figure if seen in three dimensions than it could be if seen as a two dimensional configuration. There are inherent "stresses" for depth in such a figure which determine its relative orientation in space; and these stresses are in no way different from the forces which lead to the organization of figures in the bidimensional plane.

20. Orbison, W. D.: Shape as a Function of the Vector-Field, Am. J. Psychol. **52**:31, 1939.

21. Brown, J. F., and Voth, A. C.: The Path of Seen Movement as a Function of the Vector-Field, Am. J. Psychol. **49**:543, 1937.

22. Köhler, W., and Wallach, H.: Figural After-Effects: An Investigation of Visual Processes, Proc. Am. Philos. Soc. **88**:269, 1944.

23. Goldstein, K.: The Organism, Evanston, Ill., American Psychological Review, 1939.

24. Lashley.[63] It should be noted that both these critics of the specific vector-field terminology are otherwise in agreement with certain main principles of the gestalt theory

It may be for this reason that these more recent developments of the gestalt theory have played no role in the analysis of pathologic material. A further, more obvious reason can be found in the relative scarcity of new cases [25] in the period between the two world wars. Except for the continued research of such investigators as Goldstein and Jablonski [17b] and von Weizsäcker,[26] interest in the description of disorders in the visual perception of space lagged until recently, when new material appeared among the casualties of the second world war.[27] Brain,[28] in presenting such new cases, reviewed some of the earlier contributions to the subject and gave the first inclusive clinical classification of disorders in the organization of visual space. In his interpretations of these disorders, however, he limited himself to a brief reference to the traditional theories of space perception.

In our own study of battle casualties of World War II, we therefore endeavored to test in some detail the applicability of a field theory to specific forms of spatial disorientation resulting from cerebral trauma. In the following reports, we shall consider 2 of the 12 cases which were characterized by a specific disability to localize objects in a limited portion of the field of vision. These cases were chosen because their syndromes were somewhat complementary.

In the analysis of the disorders in these cases by means of special tests, major emphasis was placed on the modifications in perceptual functions (positive symptoms) rather than on a mere demonstration of any specific deficiency or loss.[29] Specifically, we examined for the following factors: 1. Residual visual function: (*a*) form discrimination; (*b*) color perception; (*c*) after-imagery; (*d*) tachistoscopic efficiency;

25. (*a*) Halpern, F.: Kasuistischer Beitrag zur Frage des Verkehrtsehens, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:246, 1930. (*b*) Laubenthal, F.: Zur Pathologie des Raumerlebens, unter besonderer Berücksichtigung des Sehraums, ibid. **162**:202, 1938. (*c*) Scheller, H., and Seidemann, H.: Zur Frage der optisch-räumlichen Agnosie, Monatschr. f. Psychiat. u. Neurol. **81**:97, 1931. (*d*) Riddoch, G.: Visual Disorientation in Homonymous Half Fields, Brain **58**:376, 1935. (*e*) Kanzer, M., and Bender, M. B.: Spatial Disorientation with Homonymous Defects of the Visual Field, Arch. Ophth. **21**:439 (March) 1939.

26. von Weizsäcker, V.: Ueber eine systematische Raumsinnstörung (Der Fall H. B.), Deutsche Ztschr. f. Nervenh. **84**:179, 1925.

27. Paterson, A., and Zangwill, O. L.: Disorders of Visual Space Perception Associated with Lesions of the Right Cerebral Hemisphere, Deutsche Ztschr. f. Nervenh. **67**:331, 1944.

28. Brain, W. R.: Visual Disorientation with Special Reference to Lesions of the Right Cerebral Hemisphere, Brain **64**:244, 1941.

29. (*a*) Jackson, J. H.: On the Evolution and Dissolution of the Nervous System, Lancet **1**:555, 649 and 739, 1884. (*b*) Head, H.: Aphasia and Kindred Disorders of Speech, New York, The Macmillan Company, 1926, vol. 1, pp. xvi and 550; vol. 2, pp. xxxiv and 430. (*c*) Goldstein, K.: After Effects of Brain Injuries in War, New York, Grune & Stratton, Inc., 1942. (*d*) Klüver, H.: Functional Significance of the Geniculo-Striate System, Biol. Symposia **7**:253, 1942.

(*e*) fusion of visual flicker; (*f*) ability to obtain stroboscopic effects, and (*g*) phenomenal speed of a stimulus moving at standard speed.

2. Visual perception of spatial relations. This was evaluated by means of (*a*) pointing tests; (*b*) bisection of lines; (*c*) standard tests of monocular and binocular perception of depth, including the three string experiment, tests of fusion ability and stereoscopic tests and (*d*) tests for perception of shape and size at varying distances.

3. Intellectual functions pertinent to generalized orientation in space, as manifested in (*a*) map making, (*b*) route finding, (*c*) drawing and copying, (*d*) grouping and sorting of objects and (*e*) body scheme function.

General examination included neuropsychiatric evaluation and psychometric and Rorschach studies.

REPORT OF ILLUSTRATIVE CASES

CASE 1.—A 22 year old lieutenant in the United States Marine Corps was caught in a burst of shrapnel during the invasion of Saipan on June 15, 1944. He was hit simultaneously on the right side of his head, on the left hand and in the axilla. As soon as he was struck, he had a sensation of being "clubbed." There was sharp pain on the right side of his head, and he had the impression of being blinded. He staggered around with eyes closed, heard the men of his company calling for him, fell down on his knees and lost consciousness when he struggled to rise.

Three days later, when he thought he regained consciousness, he saw a chaplain standing on his right and a medical officer on his left. At this time he was tormented by a peculiar sensation that the entire left side of his body "just wasn't there." During the following days this impression predominated, but it was sometimes replaced by an intense feeling of numbness and coolness over the left side of the body. At other times the left side was oversensitive. By looking at the extremities on his left, he could satisfy himself that he was able to move them. However, he was never aware of any active or passive motion on that side, except by using his visual sense. There were no illusory feelings of motion. The gross sensory disturbances, especially the impression of absence of the entire left side, persisted after an operation, which was performed on July 31, 1944. At that time, there was a granulating wound with slight drainage within a defect in the right parietal area of the skull. Roentgenographic studies revealed numerous tiny fragments of bone embedded in the brain substance within an area of laceration in the right motor cortex (fig. 1). The destruction extended posteriorly into the sensory area (fig. 1).

At operation, twenty-two fragments of bone, varying in depth from ½ to 2½ inches (1.5 to 6.5 cm.) beneath the outer surface of the brain, were removed. A small abscess lying deep against the wall of the lateral ventricle was evacuated. After this operation, the patient showed left hemiplegia, weakness of the left side of the face and loss of kinesthesia and complete astereognosis on the left. The hemiplegia improved steadily during the next twelve months. The patient was returned to limited duty and was eventually able to typewrite, swim and run, and even qualified as a marksman. Off duty, he piloted a private plane.

This remarkable compensation of his defects contrasted strangely with the objective neurologic findings, as established on Nov. 1, 1945, when he was first

seen by us. There was hemiparesis of the left side of his body, with all the classic signs of involvement of the pyramidal tract. The muscles of the left leg were atrophic. The hand and foot were cooler on the left side than those on the right and often dripped with perspiration.

Except for point localization and vibration sense, which were only slightly impaired on the left side, there were definite sensory changes, all limited to the left half of the body. Thus, pain, touch and temperature sensibility showed a defect of the cortical type. Ability to appreciate the position of the limbs (whether actively or passively assumed) was lost in the patient's toes, fingers, ankle, wrist, elbow and knee on the left side. With this, there were pronounced incoordination and pseudo-athetoid movements on the left. There was complete astereognosis on the left side, including the left side of the lips. Graphesthesia was lost in the distal half of the upper and lower extremities on the same side. Below the midthigh and over the entire left upper extremity, the patient was unable to judge the directions of lines drawn on his skin. Ability to discriminate two points applied simultaneously was

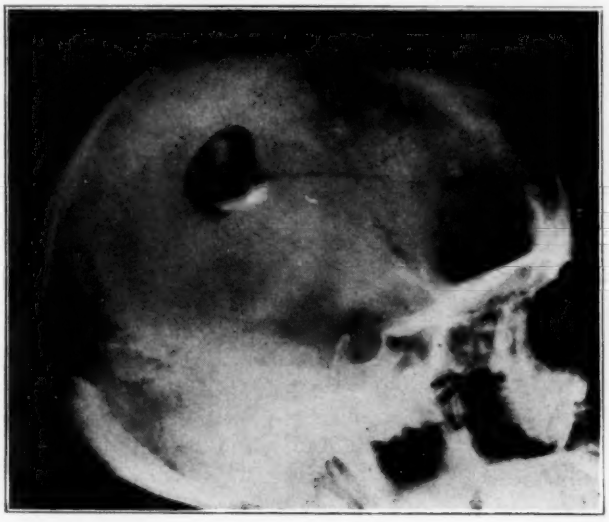

Fig. 1.—Roentgenogram of the skull, revealing a bony defect in the right parietal region.

much impaired below the level of the midthigh and over the entire upper extremity on the left side.

Repeated special tests of tactile sensibility showed that with simultaneous stimulation of corresponding points on the right and the left side of the body, there was immediate and complete "extinction" of sensations on the left. This was found even for stimulations produced by scratching with sharp objects and by application of vibrating tuning forks. Moreover, the sensory adaptation time was found to be much decreased for all sensations, including kinesthesia, on the implicated side. This was most pronounced in the acral regions. When the patient held his upper extremities outstretched and his eyes were closed, he soon lost all awareness of the presence of the left fingers and hand.[30]

Examination of the eyes showed normal fundi. In confrontation tests, the field for each eye appeared to be full. However, as soon as the patient was asked to

30. Bender, M. B.: Changes in Sensory Adaptation Time and After-Sensation with Lesions of Parietal Lobe, Arch. Neurol. & Psychiat. **55**:299 (April) 1946.

describe the appearance of objects placed in the homonymous left inferior quadrants, it became evident that definite qualitative changes in visual function had occurred in this region of the field. Functions of the rest of the cranial nerves were normal.

VISUAL SYMPTOMS

Subjective Complaints.—Until special tests were applied to the left lower quadrants of the fields of vision, the patient had only casual and nonspecific visual complaints. The subjective visual symptoms which he reported spontaneously after his injury (and which had remained unchanged to the date of these special examinations) may be described as follows: 1. He experienced increased ocular fatigue when attending the moving pictures. The patient had to shut his eyes several times during the performance to prevent images from becoming blurred or "blacked out" completely. 2. He noted a peculiar tendency for boundaries between colored fields to become indistinct; this he described as a "blurring" of colors. He said he was unable to name colors in the border region of any two adjacent color fields. 3. Blurring and visual fatigue were much more pronounced under conditions of low or artificial illumination. He did not complain of any increase in the discomfort which is normally caused by glare. 4. He was finally aware of an abnormal tendency to rely on central vision alone.

Perimetric and Tangent Screen Studies.—The perimetric fields taken under our standard conditions (distance, 33 cm.; 1 degree white and red targets; illumination, 7 foot candles) revealed no peripheral cuts for form or motion. However, the fields for red showed homonymous indentations on the left, most prominent in the left inferior quadrants (fig. 2). Routine tangent screen examinations revealed no abnormalities. The tangent screen test was then modified to measure the patient's peripheral acuity, as indicated by his ability to resolve a double line in various orientations. These tests were given with targets 2 cm. long at a distance of 150 cm. (large-far constellation) and were repeated with 1 cm. targets at a distance of 75 cm. (small-near constellation). The distance was measured from the patient's eyes to the fixation marks in the center of the tangent screen. The targets were introduced radially from the periphery inward, and the point of greatest eccentricity at which the patient was first able to resolve the test lines in any given meridian was marked off.

Under these conditions, the patient's peripheral acuity was consistently inferior in the left lower quadrant. This inferiority was more pronounced for the large-far constellation than for the small-near constellation. In addition, there was a similar, but milder, contraction for the opposite, or right lower quadrants. This contraction was likewise limited to the large-far constellation. In other words, the patient's functional field, as assessed by his ability to resolve visual patterns, was shrinking with increasing distance, even though the linear dimensions of the test objects were increased in direct proportion to the increasing distance.[31]

Tachistoscopic Examinations.—Results of repeated tachistoscopic tests were consistent with the finding of a relative homonymous defect in the left inferior

31. Bender and Teuber.[1b] This effect was noted for normal subjects, at least within this range and with such test objects as were employed in our setting. In the phychologic literature the effect is known as the Aubert-Förster phenomenon (Aubert, H.: Physiologie der Netzhaut, Breslau, E. Morgenstern, 1865. Jaensch.[40a] Freeman, E.: Anomalies of Visual Acuity in Relation to Intensity of Illumination, Am. J. Psychol. **42**:287, 1930). However, for our normal control subjects, the effect was less pronounced and the shrinking of the field with increasing distance tended to be symmetric (concentric).

quadrants. With strict monocular fixation (left or right eye) and with his head in a chin rest, pictures, geometric patterns, letters and figures were exposed to the patient's central and paracentral fields. The area of projection extended 8 degrees horizontally from the center of fixation and 6 degrees vertically in either direction. The time of exposure was varied from one to one-fiftieth second, but was usually kept at one-tenth second. At this speed the patient showed a tendency to miss those portions of the slide which were exposed to the left of his median plane. The defect was most pronounced in the lower left quadrants.[32]

After-Imagery.—The methods used in testing after-images were the same as those reported in previous communications.[33]

From observations on other patients with relative defects in quadrants and half-fields, one would expect a more rapid fading of the after-image in the most involved quadrant. For this patient it was found, instead, that after monocular stimulation with either eye the after-image persisted longest (indeed, abnormally long) in the left lower quadrant. The patient had also great difficulty in obtain-

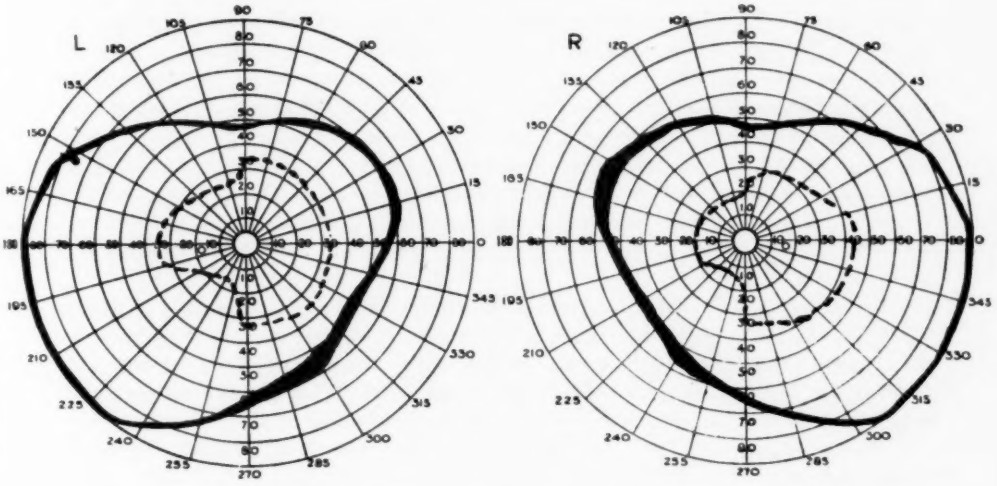

Fig. 2.—Perimetric fields of vision, illustrating homonymuos defect for color on the left side. All perimetric tests were performed under an illumination of 7 foot candles, using 10 mm. test objects at a distance of 33 cm. The outer border indicates the extent of the field for perception of movement. The broken lines indicate limits of the field for red.

ing complementary colors in the entire field after monocular stimulation. With binocular exposure, however, the patient's after-images showed the expected rapidly progressing contraction, beginning in the left lower quadrant. Motion after-images (as produced by rotating spirals)[1b] were readily obtained in any quadrant of both the monocular and the binocular field of vision.

Further Objective Indications of Relative Defect in Left Lower Quadrant.—The results of the tachistoscopic tests were further corroborated by special methods of examination of the fields such as (*a*) determination of fusion thresholds for

32. The degree of the patient's dark adaptation made no significant difference in the outcome of these tests.

33. Bender, M. B., and Teuber, H. L.: Nystagmoid Movements and Visual Perception, Arch. Neurol. & Psychiat. **55**:511 (May) 1946; footnote 1 *a* and *b*.

visual flicker in different regions of the patient's field; (*b*) assessment of phenomenal speed, by a matching procedure similar to the one applied by Brown,[34] in the central field, as well as in the four quadrants, and (*c*) measurement of thresholds for stroboscopic motion in different parts of the field. These methods consistently revealed a lowering of physiologic efficiency in the patient's left homonymous fields, especially the inferior quadrants.[35]

Gross Symptoms of Disorder in Perception in Left Lower Quadrants (Teleopsia and Micropsia).—When similar objects were exhibited to the left and right lower quadrants of the patient's binocular or monocular fields, he reported that the object in the left lower quadrant appeared (1) less brilliant, or somewhat "grayish," or (2) "farther away" than it did when exhibited to the right half of the field at the same objective distance. Usually if tested with the target at 5 to 10 degrees of eccentricity in the left lower quadrant, the patient reported that the image was about half as large as it should be, i.e., as it appeared in the center and the three remaining quadrants of the field. If the target was moved farther toward the periphery of the left lower quadrant, (3) he reported an additional shrinking; *pari passu* with the illusion of decrease in size, the perceived distance of the objects increased. Generally, this tendency toward excessive perceived distance (teleopsia) for objects presented to the patient's left lower quadrant was the most persistent symptom. The teleopsia was accompanied with an illusion of abnormal smallness (micropsia) whenever the object was familiar, that is, when the object's "true" size was known to the patient by experience (fingers, pencils) or by repeated exposure to different quadrants. With unfamiliar objects, such as outline circles or disks, he frequently experienced teleopsia with macropsia. In these instances, the objects, while "dropping back" in space, seemed to him to expand at the same time.

Finally, in addition to the patient's constant tendency to perceive objects in the left lower quadrant as if they were at a great distance (teleopsia), together with the recurrent micropsia and occasional macropsia, there was (4) a tendency to distortion of shapes (dysmorphopsia, metamorphopsia). This distortion took place only at greater eccentricity (beyond 5 degrees from the center of fixation) and was less constant and less pronounced than the previously noted perceptual disturbances.[36]

The most constant and most pronounced disturbance in the left lower quadrants of the patient's visual fields was (5) an inability to localize objects by pointing. When he was allowed to view a target in direct gaze, his pointing was always correct. Even monocularly, he showed practically no errors, which may have been due to his training as a marksman. Neither was there any gross past pointing with the eyes closed, provided the patient used the normal, or right, hand, once he had ascertained an object's position by touch or by central vision. However, if the

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34. Brown, J. F.: The Visual Perception of Velocity, Psychol. Forsch. **14**: 183, 1931.

35. Some of the special methods used in this investigation were described in previous communications.[1] As in all other cases, the relative field defect manifested itself in (*a*) an abnormal increase of phenomenal (perceived) speed, (*b*) a considerable rise in thresholds for apparent (stroboscopic) motion and (*c*) a decrease in fusion frequencies for flicker.

36. The pertinent observations on the patient's dysmorphopsia and metamorphopsia will be included in a forthcoming report on disorders in the perception of shape after injury to the brain. (See also Teuber, H. L., and Bender, M. B.: Significance of Changes in Pattern Vision Following Occipital Lobe Injury, Am. Psychol. **1**:255 [July] 1946.)

patient was asked to point at a target exhibited in the left lower quadrant a few degrees off his center of fixation, he invariably pointed too far, and at the same time tended to stray to the left, or toward the periphery of the field. This form of past pointing was always more pronounced in the sagittal than in the coronal plane. (Occasionally, he would err by pointing at a roughly corresponding location in the right lower quadrant, thus showing a form of optic allochiria, or transposition of the image into the opposite, or better, region of the field.)

Since the patient's disorientation in visual space seemed highly specific (in the absence of any symptoms of general disorientation in space), and practically limited to the homonymous left lower quadrants, efforts were made to determine more exactly the extent of these difficulties in the visual perception of spatial relations.

Bisection of Lines.—A constant difference in "space values" between the right and the left halves of the patient's fields seemed to be demonstrated by his performance in bisecting lines.[37] The patient was instructed to bisect lines presented in different meridians. 1. In the first series of experiments, he was told to fix at a point which he assumed to be in the middle. With binocular and monocular viewing of a horizontal line 152 mm. long, he made constant errors in his attempts at bisection (fig. 3 *A*). It is inferred that the portion located on the defective (left) side must have appeared to him longer than that on the right side. He was not aware of this inequality; all he noted was the fact that the left side appeared farther away and "sloping outward." 2. The patient was then asked to bisect a line with monocular and binocular fixation on one end of the line. The resulting bisections are presented in figure 3 *B*, with the line in the four main orientations. It will be noted that the patient erred practically without exception in "typical"

37. If a normal subject is told to bisect a line oriented in the horizontal meridian, with monocular fixation on its presumed midpoint, he will usually make the temporal portion too long (Kundt's bisection error [Kundt: Ann. d. Physik. **120**:118, 1863; cited by Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 1]). If, instead, he is told to fix at one end and then to bisect the line, he will tend to make the peripheral portion too long, regardless of in which meridian the line is oriented. The older theories of "space values" and their distribution on the retina (Hering.[39] Hillebrand, F.: Die Stabilität der Raumwerte auf der Netzhaut, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **5**:1, 1893. Witasek, S.: Psychologie der Raumwahrnehmung des Auges, Heidelberg, C. Winter, 1910. Tschermak, A.: Augenbewegungen, in Bethe, A.; Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1931, vol. 12, pt. 1, pp. 1001-1094) interpreted this tendency as an indication of an unequal distribution of space values on the retina: At the periphery, space values are packed less densely than in central areas of the retina. Hence, a given line, when projected onto the periphery, will appear shorter than it appears in central vision. For this reason, on attempted bisection of the line, the most peripheral portion will be made too long. When a hemianoptic subject is asked to bisect a horizontal line, with fixation on its presumed midpoint, he usually errs in the same direction as a normal subject but to a much greater extent (Liepmann, H., and Kalmus, E.: Ueber eine Augenmasstörung bei Hemianopikern, Berl. klin. Wchnschr. **37**:838, 1900). Best,[9a] who subjected to systematic investigation such errors in bisection following injury to the brain, found both "typical" errors and errors in the opposite direction, or "atypical" errors. Fuchs confirmed Best's observations and systematized them in terms of his theory of functional foveas, or pseudofoveas, in defective visual fields.[7] "Typical" errors were found to be characteristic of cases of hemianopsia; "atypical" errors predominated in cases of hemiamblyopia and quadrant amblyopia.

fashion when the line was oriented in the horizontal meridian to the patient's left. A similar error was made when the line lay in the vertical meridian (with the patient fixing on the upper end). That is, in these orientations, the peripheral portion was made too long. Although overestimations of this sort are made by normal subjects, they were evidently excessive in tests on this patient.[38]

On the contrary, the patient consistently made an "atypical" error (i. e., he made the peripheral portion too short) when the line was oriented to the right of

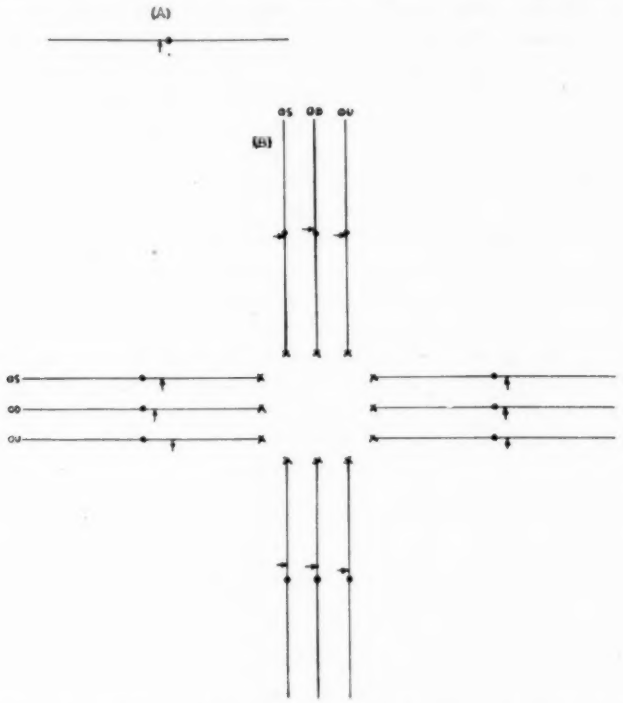

Fig. 3.—Bisection of lines: *A*, result of patient's attempts to bisect a horizontal line (15.2 cm. long) on scanning freely the whole line and fixing on the presumed midpoint. With binocular, as well as with monocular, vision the presumed midpoint was placed too far to the left. *B*, result of patient's attempts to bisect a line, using the right eye (*O.D.*), left eye (*O.S.*), or both eyes (*O.U.*), while fixing strictly at one end of the line (*X*). Each of the lines (which were all 15.2 cm. long) was presented consecutively in the horizontal and vertical meridians (i.e., to the right and the left of the points of fixation, as well as above and below these points). Each test line appeared on a gray cardboard background in the patient's coronal plane, at a distance of 40 cm. from the eyes. The drawing is a composite picture and is intended to reveal the uniformity of the displacement. The dot in the line is the true midpoint. The arrow indicates the place where the patient assumed the midpoint to be.

38. Owing to limitations inherent in the setting, these tests could not be repeated often enough to furnish us with adequate estimates of the patient's variability. Generally, patients err consistently until they become aware of their constant errors. In their attempt to correct the errors, their pointing and bisecting may become much less predictable. The illustrations represent, therefore, only the characteristic behavior on first testing.

his fixation point along the horizontal meridian. In this instance his response was the opposite of that of a normal subject. Apparently to his left, the most peripheral portion seemed to him longer than did the portion in paracentral and central vision.

Three String Experiment.—In studying binocular depth perception in our patients, we used an adaptation of the classic three string experiment. In this setting,[39] the subject views three vertical black threads suspended behind an occlusion screen. Behind the threads is a gray background. The three threads are equidistant from each other and are situated in the subject's coronal plane. In the standard experiment, the subject fixes binocularly on the central thread. In successive trials, this thread is presented (*a*) in the same plane as the other two threads, (*b*) slightly farther away than the other two and (*c*) slightly closer than the other two. The subject's task is to judge whether all three threads are actually in one plane or whether they form a concave or convex wedge in relation to his line of regard. In a modification of the classic experiment, the threads are first presented in the coronal plane. The patient is then moved to the right or to the left of the original line of regard. After he has been moved to the side, he is specifically instructed to fix at the middle thread and to indicate how the strings should be readjusted in order to bring all the threads in what he considers his coronal plane.

The two diagrams in figure 4 give characteristic results after the patient was thus moved 15 degrees to the right, and later 15 degrees to the left, of his original central position.[40] In each instance the results showed that the target (thread) on the left seemed "too far." This teleopsia induced the patient to bring the left thread closer to him, so as to make all three threads appear in what he considered his coronal plane. However, as the diagrams indicate, the distortion in the patient's perception of visual space was not limited to his left side. Under the conditions specified in the experiment, he showed a complementary change in his right field of vision The thread on the right had to be moved back beyond the true coronal plane (perpendicular to the line of regard in the new position). It will be noted that, regardless of the patient's new position (whether to the right or to the left of the original position), the right thread was moved behind the true coronal plane.

In other words, the patient rearranged the threads within a plane which was at an angle to the true coronal plane. Regardless of the patient's position, the left thread was placed objectively "too close" and the right thread "too far." The patient's behavior thus suggested that his entire subjective coronal plane had rotated around the median, and hence no longer coincided with the "true" coronal plane. Accordingly, whenever the threads were not readjusted to satisfy the patient but were kept, instead, in the "true" coronal plane, the patient experienced them as though rotated through a sizable angle (15 to 30 degrees) around the median. The thread to the patient's left then appeared to him much farther, and the thread to the right much "closer," than they would have appeared to a normal observer.

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39. Hering, E.: Spatial Sense and Movements of the Eye, translated by C. A. Radde, Baltimore, Williams & Wilkins Company, 1942, pp. xii and 221.

40. (*a*) Jaensch, E. R.: Ueber die Wahrnehmung des Raumes, Leipzig, Johann Ambrosius Barth, 1911, p. 488. (*b*) Normal observers, on using binocular vision, have little difficulty in arranging the three threads in the coronal plane. Within the range tested, there is usually a slight tendency to make the arrangement concave, but the departures from the true coronal plane rarely exceed 2 to 3 mm. When a normal observer is placed to one side (right or left) of his original line of regard and the strings are kept in their original position, a curious phenomenon is noted. The area defined by the three strings appears to the subject no longer as a plane but as slightly concave. This effect was known to Jaensch, who related it to such phenomena in normal visual perception as the curved appearance of the sky.

An incidental observation during these tests was a certain lability of localization in the sagittal plane. When all three threads had been placed objectively in the coronal plane, the patient reported that the center thread seemed to move back and forth in the sagittal plane. Occasionally, the two outer threads "blacked out." More frequently, only the thread to the left seemed to disappear and reappear at short, irregular intervals. All this occurred even with monocular vision.

In summary, it may be stated that these special tests confirmed the presence of teleopsia, particularly in the left lower quadrants of the fields of vision. This was found on monocular and binocular tests. (*a*) Teleopsia was the most consistent finding, whereas the concomitant changes in size and shape were not as constant. The latter depended largely on the constellation of the presented objects. (*b*) The teleopsia itself could be modified in its extent by certain changes in the stimulus pattern. (*c*) Under certain conditions, the disorders in space, size and shape on the left side sometimes extended to involve the rest of the field. Involvement of the right side of the field was transient and much less pronounced than on the left side.

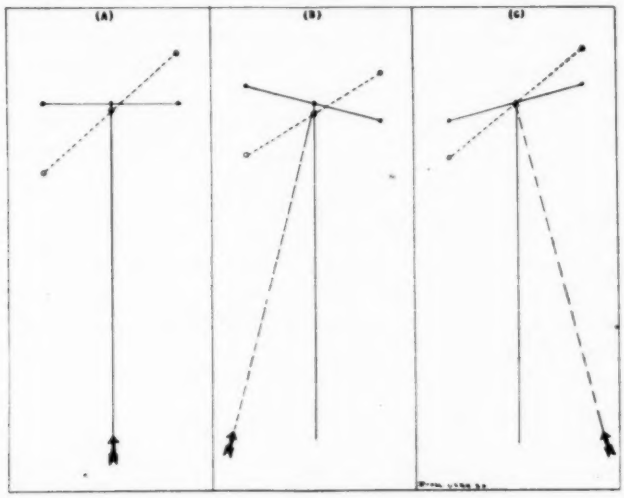

Fig. 4.—Schematic drawing of the patient's attempts to place the three strings in the frontoparallel, or coronal, plane. The arrow indicates the position and direction of the patient's eyes. The solid line with dots indicates the true coronal plane, the broken line with circles shows what the patient assumed to be the coronal plane. In *A* the patient views the threads in the line of regard: in *B* he views the threads 15 degrees to the left, and in *C*, 15 degrees to the right of his original line of regard.

Visual Stimulations Without "Framework."—Even in normal subjects, the structure of visual space may show lability or become distorted if the visual framework is missing or if the postural mechanisms are disturbed. Thus, a single light in the dark has no particular localization, but after a certain period of latency begins to describe illusory motions (autokinetic movements), which may eventually involve the patient's postural organization, so that even a patient's own body, the chair on which he sits or the floor begin to sway and turn in the dark room.

Conversely, a predominance of postural components over purely visual factors in localization is brought out in normal subjects by presenting to them a single luminous vertical line in a totally dark room. If the subject tilts his head to the left, the line will seem to be inclined correspondingly to his right, and vice versa

(Aubert phenomenon). In normal surroundings, a tilt of the eyes, head and trunk will not produce an apparent tilt of the perceived vertical line.

With our patient, autokinetic movements were not at random in all directions of the field, as they are with the normal subject. Instead, the light drifted persistently upward and to the patient's right, or, in other words, away from the most affected region of his field. The Aubert phenomenon was likewise modified, and in the same manner. When the patient tilted his head to the left, the presented vertical line seemed to him to tilt to the right. This is the most usual normal reaction. However, when he tilted his head to the right, the line seemed to him inclined to his right side (and not his left, as expected).

Further tests in a dark room with single stimulus patterns (luminous lines and circles) revealed that the patient's ability to localize objects in his left lower quadrants was frequently beset by the same difficulties that he experienced in daylight.[41]

When a single luminous pattern was exhibited alternately to the patient's left lower quadrant and to his right lower quadrant, he pointed correctly on the right, but on the left he pointed considerably to the left and beyond the test object. Thus, even a single light surrounded by total darkness was displaced by the patient in the coronal, as well as in the sagittal, plane. However, under these conditions, the teleopsia was not accompanied with changes in the object's apparent size and shape.

Stereoscopic Tests.—Using a simple refracting stereoscope, the patient obtained binocular fusion and normal depth effects. However, in the lower left sector of the fused image fusion was ill sustained, and the image appeared faded. In the remaining quadrants no abnormalities were reported by the patient.[42] These results were obtained irrespective of the type of figure used in the fusion tests.

Intellectual Functions Pertinent to Orientation in Space.—The patient was capable of making maps and showed considerable skill in the interpreting of blueprints. (As we have already pointed out, he was able to navigate a plane.) His drawing and copying ability for bidimensional and tridimensional patterns was within normal limits.

However, on certain visual-constructive subtests of the Wechsler-Bellevue scale, the patient was unable to perform according to his intellectual level (as indicated by an intelligence quotient of 126). He exceeded the time limits and failed on surprisingly simple tasks. Especially in block tests, there was a curious tendency for errors to appear in the left half, and most frequently in the left lower sector of the patterns.

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41. Maintenance of the patient's forward fixation in the dark room was accomplished by instructing him to face an intermittent sound coming from a source in front of him Previous tests of auditory localization and associated movements of the head and eyes in this patient had shown that his performance was approximately normal in these respects.

42. It should be borne in mind that even wtih the normal subject, fusion may be unequally sustained in different sections of the binocular field. Such inequalities may be produced by the usé of conflicting contours in the stereoscope. If a horizontal line is presented to one eye and a vertical line to the other, the fused binocular image is that of a cross. In the area of intersection of the two lines, fluctuation in the distinctness of the image will occur. This fluctuation has been interpreted as a sign of binocular rivalry, which can apparently be limited to the area of intersection. Such localized rivalry can be demonstrated not only in the center of the field but in any other portion of the field in which there are intersecting or "conflicting" contours.

Grouping, sorting and other tests of abstract behavior[43] failed to reveal any general impairment in his intellectual organization which could have contributed to the specific difficulties in visual space perception. There was no right-left disorientation or apraxia. Except for the changes already noted in the sensory status of the neurologic examination, the patient had no gross disorder of the body scheme.

Comment.—A number of points in this case are worth emphasizing.

1. The disorientation in visual space was largely limited to homonymous (left lower) quadrants of the field of vision.

2. Except for a slight contraction for color, the perimetric fields and tangent screen examinations revealed no gross defects.

3. However, special tests showed that the integrity of the field was only apparent. Procedures such as the measurement of fusion frequencies of visual flicker, determination of thresholds of stroboscopic motion, assessment of phenomenal speed and evaluation of after-imagery disclosed a definite alteration in visual function, particularly in the left lower quadrants, where there was also spatial disorientation.

4. The spatial disorientation occurred in all three dimensions, but it was most pronounced in the sagittal plane. It was thus manifested not as a lack, but as an excess, of "depth," i. e., teleopsia. The teleopsia was accompanied with changes in apparent size and shape.[44]

5. The errors in localization in the affected field were not at random. They followed definite trends, as shown by tests of pointing and bisection of lines. The patient consistently past pointed to the left and beyond the target. In bisecting lines, he always greatly overestimated the peripheral portion of lines presented in his left field of vision. It can thus be inferred that the coordinates of the subjective visual field had undergone a deformation. The presence of such a systematic distortion was further demonstrated by the three string experiment. In this experiment (and under other, similar conditions in which both halves of the field of vision were simultaneously stimulated) the patient's performance suggested that the subjective coronal plane was rotated as a whole. The direction of the rotation of this plane was "away from" the patient on his left and "toward him" on his right. With this, there were occasional alterations in apparent size and shape in the right, as well as in the left, half of the field of vision.

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43. Goldstein, K., and Scheerer, M.: Abstract and Concrete Behavior: An Experimental Study with Special Tests, Psychol. Monogr. **53**:151, 1941.

44. The observation that teleopsia in the case of unfamiliar objects was associated with an apparent enlargement (macropsia), rather than with micropsia, might have important theoretic implications. However, most of these observations were made with indirect vision. Under such conditions, there is little, if any, constancy of size, even with normal subjects. Comments on the associated changes in size will therefore be limited to the second case, in which similar findings could be obtained, even with macular vision.

6. Conversely, changes in the actual size of the presented object modified the teleopsia. The alterations in the patient's subjective visual space perception were therefore not absolutely constant. They could be influenced, even reversed, by changes in the total stimulus configuration.

7. The more the total stimulus configuration was simplified, the more apparent were the persistent tendencies toward deformation in the subjective coordinates of visual space. When a visual framework was practically absent, as on stimulation with a single luminous target in a totally dark room, the resultant illusory motions of a single light, and illusory inclinations of a luminous vertical line, were always to the right, or away from the implicated (left) region of the patient's field.

8. The case under consideration gains in theoretic significance if one bears in mind that there was no intellectual deficit, no gross spatial disorientation, executive disorder or agnosia.[45] The perceptual disturbance was practically limited to the field of vision.

9. In spite of the limited nature of the disorder, the extraordinary amount of successful compensation of the defect remains a problem. The patient's performance on tests with the stereoscope may perhaps help to explain it. Under the additional stress of binocular fusion, there were fluctuation and extinction of that portion of the fused image which was exposed to the homonymous left lower quadrants. Possibly this automatic extinction led, in everyday vision, to elimination of the disturbing teleopsia and the associated abnormal perceptions.

In this instance, then, extinction would seem to have a teleologic nature. However, as we have pointed out elsewhere,[1a] extinction may just as readily lead to serious impairment of vision, as, for example, by changing hemiamblyopia into what amounts to complete hemianopsia.

45. The only inkling of a more serious involvement of gnosis and praxis might be seen in the patient's difficulties with the Kohs block test. His tendency to make errors oftenest in the most implicated (left lower) quadrant demonstrates the close clinical relation between central disorders of vision and defects of "visualizing" (visual memory). One is reminded of Niessl von Mayendorf's unorthodox view (Niessl von Mayendorf, E.: Zur Lehre von der Seelenblindheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:345, 1935; **159**:284, 1937) that pattern vision proper and "visualizing" (or visual memory) have the some cortical substrate.

(To Be Concluded)

POLIOMYELITIS

Study of an Epidemic of Forty Cases in Key West, Fla., May-August 1946

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AND
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ON MAY 23, 1946 an epidemic of poliomyelitis began on the island of Key West, Fla., 120 miles (192 kilometers) from the mainland and 170 miles (272 kilometers) southwest of Miami. During the next month and a half at least 38 cases of clinical poliomyelitis developed, 36 of which were of the paralytic type. One month later, on August 4, 2 other cases occurred.

The population of Key West at the time of the epidemic was about 14,000 civilians and about 3,500 Naval personnel and their families.

Ten of the first 11 patients were treated at Jackson Memorial Hospital in Miami; the remaining 28 patients (except for 2, whose disease developed while they were en route to California) were observed, their illness diagnosed and treatment administered at the United States Naval Hospital in Key West. There had been no previous epidemics of poliomyelitis in Key West, and the average incidence of the disease for the past ten years had been only 1 case per year.

The hospital set up a special poliomyelitis unit for the Key West area. One hundred and ninety persons suspected of having the disease, in addition to the 40 patients with a positive diagnosis, were examined and observed. Of these, 11 were believed to have abortive poliomyelitis, and 22, probable abortive poliomyelitis, and over 100 had symptoms of a disturbance which remained undiagnosed. The last group complained of some combination of the following symptoms: fever, headache, muscular pains, neck ache, backache, dizziness, general malaise, sore throat and transient weakness of an extremity. One or more examinations of the spinal fluid were made on most of these patients, without evidence of the disease. None of these patients, however, is included in the list of 40 patients with clinical poliomyelitis.

From the Medical Service, United States Naval Hospital, Key West, Fla.

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The incidence of verified cases in this epidemic was 2.3 per 1,000, or 230 per 100,000, of the population.

Some of the findings in this epidemic were unusual. The age and sex ratios for the civilian group differed from those for the service personnel and their dependents. Of the 40 patients, 19 were civilians, 16 were dependents of service personnel and 5 were service personnel. Although 17, or 42.5 per cent, of the total number of patients were adults (19 to 33 years of age), 73.7 per cent of the patients in the naval families involved were adults, whereas only 10.5 per cent of the civilian patients were adults.

Thirteen (68.4 per cent) of the patients in the Navy group were in officers' families, although the ratio of officers to enlisted men was about 1:8. Eight of the 19 service personnel and dependents with the disease were wives of officers and 2 were wives of enlisted men.

TABLE 1.—*Distribution of Cases of Poliomyelitis According to Age Groups*

Age, Yr.	Service		Civilian		Total No.	Percentage of Cases
	M	F	M	F		
Under 1	1	0	0	0	1	2.5
1 to 2	1	1	1	2	5	12.5
2 to 3	0	0	0	2	2	5.0
3 to 4	1	0	1	0	2	5.0
4 to 5	1	0	2	1	4	10.0
5 to 10	0	1	3	1	5	12.5
10 to 15	0	0	3	0	3	7.5
15 to 20	1	1	0	2	4	10.0
20 to 25	0	5	0	1	6	15.0
25 to 30	1	3	0	0	4	10.0
30 to 33	2	2	0	0	4	10.0
Total	8	13	10	9	40	100.0

There was a strong history of contact in this group. This aspect will be discussed later. Of the Navy patients, 2 were officers (lieutenant commanders) and 2 were enlisted men, all of whom lived in the city of Key West. The other, a Wave on the hospital staff, lived in the hospital barracks.

Of the 40 patients, 22 were females and 18 males. Of the adults, 13 were women and 4 men. The youngest patient was 7 months old; 4 patients were 30 years of age or older.

Although the expectancy of paralytic poliomyelitis during pregnancy has been given as less than 1 in 1,000 cases of poliomyelitis and less than 1 in 50,000 pregnancies,[1] 6 of the women in this epidemic were pregnant. A seventh was three weeks post partum at the time of admission.

There were 3 deaths (1 adult and 1 child in the Navy group and 1 adult in the Army group), a mortality of 8.3 per cent of the para-

1 Aycock, W. L.: New England J. Med. **225**:405, 1941.

lytic patients. Five of the first 10 patients were respirator patients; there were 7 respirator patients in all.

There were 3 instances in which 2 positive cases occurred in the same family (6 patients). Thirteen of the 34 remaining patients gave a history of febrile illness in one or more members of the family at the same time which, as described, could have been a mild abortive form of the disease. In 3 patients acute symptoms developed just after they left Key West (2 en route to California and 1 to Palm Beach).

No cases were reported among the Negro population. Only 8 of the 19 civilian patients were natives of Key West. All but 1 of these natives were children, all under 5 years of age. The only adult was the pregnant mother of 1 of the patients.

EPIDEMIOLOGY

The frost-free city of Key West, which occupies most of the terminal island of the chain of Florida Keys, is 4 miles (6.4 kilometers) long and 1½ miles (2.4 kilometers) wide. The northeastern half of the island is rimmed by Roosevelt Boulevard. In the northern part of this half of the island is located the large, wartime (civilian and Navy) Poinciana housing project, where 13 cases were reported. The entrance to the island is at this northeastern end, where the Naval Hospital is located. Just below the southeastern end of Roosevelt Boulevard is the small Rest Beach housing project (75 units), limited to Naval officers' families, where 6 of the cases of poliomyelitis developed.

The climate is semitropical.

The milk supply and at least 90 per cent of all other supplies for the various Naval activities and the city come from the Miami district.

It is seldom possible to narrow the mode of transmission of the virus of poliomyelitis to a single factor. Modes of transmission which have had various degrees of importance in the past, and which were considered in this epidemic, were water, food, milk, flies, sewage pollution and direct contact.

Water.—The water supply, delivered by pipe line from Florida City, is chlorinated at the source, rechlorinated en route and again rechlorinated by the city and each naval station before use. The present water line was built in 1944. Before that time the natives had to depend on rain water, which they stored in cisterns. Many of these cisterns are cross connected with the main water lines which enter these homes. Eight hundred to 1,000 cisterns are still in use, and few are properly closed. It is possible that the main water supply may be contaminated by these cistern cross connections: however, samples of water have been tested weekly and have always been found to fulfil the standard requirements of water analysis.

Sewage Disposal.—The main method of sewage disposal is by septic tank or cesspool, since less than 30 per cent of the homes are connected with the sewage disposal lines. Eight civilian and 4 Navy patients lived in homes where sewage was disposed of by a septic tank or cesspool.

Before the epidemic started, the raw sewage was pumped through sewer lines with two outlets: one, on the northeast side of the island, into the Gulf of Mexico, with an emergency by-pass into Garrison Bight Yacht Basin, a shallow, semi-inclosed body of water; the other, extendng 600 feet (182 meters) from the southeastern end of the Key into the Atlantic Ocean near South Beach, Fort Taylor Officers' Club Beach and Rest Beach, which are the island's principal bathing beaches. Tidal action is slight here, and gross sewage was often observed close to shore. Subsequent to the onset of the epidemic the sewage was pumped into settling tanks and the effluent chlorinated; pumping of sewage into Garrison Bight Yacht Basin was discontinued.

Garbage.—Both wet garbage and trash are hauled to a "dump" near United States Highway no. 1 on Stock Island, the next proximal Key. An attempt is made to burn and to bury the collection with one bulldozer; most efforts at burial are futile, since part of the "dump" is on swampy land. Garbage is collected once a week except in the federal housing units, where it is collected three times a week. In the housing units most garbage cans have poorly fitting lids, and the cans often overflow. In the city, most of the lids of the garbage cans were missing; others were badly bent.

Milk.—The milk, which is supplied by two dairies, is tested regularly. It is trucked in from the Miami area.

Flies.—Flies are prevalent throughout the city, but not in larger numbers than usual. Chickens, horses and numerous dogs and cats are kept, improperly, within the heavily populated parts of the city.

A Navy plane began spraying the island with DDT (4,4'-dichlorodiphenyltrichloroethane) as soon as the epidemic started. This spraying has been continued at frequent intervals and has greatly reduced the fly and mosquito population.

EPIDEMIOLOGIC HISTORY

Repeated "direct contact" was the most obvious and important common denominator in at least 18 of the cases, which included five small groups of patients. In other cases, flies and poorly handled garbage seemed to be particularly incriminated.

Swimming in polluted water was another distinct etiologic possibility. Eighteen of the 40 patients had been bathing at Rest Beach or South Beach during the two or three weeks preceding the onset of

their illness. (For 9 patients information on this point was not available.) These two beaches, where tidal action is slight, were located near the sewage outlet.

Table 2 gives the results of bacteriologic examination of samples of water from the principal beaches and swimming pools in this area.

Since this analysis, the sewage effluent has been chlorinated, and at the present time samples show no evidence of pollution. Swimming was prohibited at all service pools and at the Officers' Club beach as soon as the epidemic began.

The occurrence of over 1 colony of the gas-forming Escherichia coli (Bacillus aerogenes) group per 100 cc. sample from deep salt water and more than 5 colonies per 100 cc. sample from surface water is evidence of pollution. It is to be noted that from all the sites except Municipal Pool, Naval Air Station Bathing Beach and the Naval Hospital the water showed gross pollution. The greatest pollution

TABLE 2.—*Bacteriologic Examination of Water (July 22, 1946)**

Salt Water (100 Cc. Samples) Collected from	Final Presumptive Test, Cc.				Confirmatory Test, Cc.			
	10	1.0	0.1	0.01	10	1.0	0.1	MPN †
Rest Beach Pond	5+	3+	0	0	5+	3+	...	79
Municipal Pool	0	0	0	0	...	...	...	...
Weaver's Cabins	5+	3+	1+	0	5+	3+	1+	110
Poinciana Lake	5+	5+	0	0	5+	5+	...	240
Rest Beach	5+	4+	4+	0	5+	4+	4+	350
Officers' Club Beach	5+	5+	3+	0	5+	5+	5+	920
Garrison Bight Yacht Basin	5+	5+	4+	0	5+	5+	4+	1,600
Naval Hospital	0	0	0	0	...	...	...	...
Naval Air Station Bathing Beach	0	0	0	0	...	...	...	...

* Furnished by the Miami Branch State Board of Health.
† MPN means maximum probable number. Other values are expressed as the number of colonies.

(expressed as the maximum probable number) occurred in Garrison Bight Yacht Basin and the Officers' Club, which are in closest proximity to the sewage outlets.

The last important factor seemed to be visits to Miami, where there were a number of cases of poliomyelitis. Thirteen of the patients had either been in Miami within the preceding three weeks or had had Miami visitors in their homes. At least 5 of the patients apparently contracted their disease in Miami. Miami, Fla., and Habana, Cuba, were the two cities of size nearest Key West. The epidemic in Key West began on May 23, when the peak of the Miami epidemic was reached. There was also an epidemic at this time in Cuba (90 miles [144 kilometers] away by air). In the next six weeks 37 verified cases developed. The cases were fairly evenly distributed throughout this period. The longest interval between the appearance of cases was five days. The greatest number of cases to appear in one day was 5.

A month after the epidemic was apparently over, 2 new cases, those of a man and a pregnant woman, occurred.

The development of the epidemic may be briefly sketched.

The first patient, a 2 year old girl, was the daughter of an iceman who had been making regular trips to Miami to visit his wife (who had a febrile illness not diagnosed as poliomyelitis). This patient lived in downtown Key West.

Eight of the next 9 patients (cases 2, 3, 4, 6, 7, 8, 9 and 10) were from the Poinciana area. Five of these 8 patients (all children) had played together frequently and had become ill with clinical signs of poliomyelitis about the same time. Three of them had played near a large pool of stagnant water in the backyard, which was subsequently condemned by the city. Three had been in swimming at Rest Beach or South Beach. Three had made recent visits to Miami or had had visitors from Miami.

The patient (case 5) who did not live in Poinciana was the wife of an officer aboard one of the submarines and lived at Rest Beach. Ten days later the executive officer aboard the same submarine, a friend of this patient, had onset of acute bulbar poliomyelitis (case 17). Significantly, two months later the wife of an enlisted man on the same submarine was admitted with poliomyelitis (case 39). The families of patient 5 and patient 17 were in frequent contact. The children of patient 19 played frequently at the home of patient 5. Two weeks after patient 5 was admitted, patients 19, 20 and 21 were admitted with acute preparalytic poliomyelitis. These 3 patients were pregnant women, good friends, 2 of whom were next door neighbors at Rest Beach; the third lived in Poinciana. They had been at parties together and were frequent visitors at each other's homes. Ten days after patient 19 exhibited acute symptoms of poliomyelitis, her husband (case 28) presented acute symptoms of the disease and died five days later, of the bulbar form.

Patient 11 was the wife of an enlisted Navy man. She had been in Miami two days before the onset of her illness. She had no history of contact, nor did patients 12 and 14 (both children). Patient 12, a 10 year old boy, had arrived in Key West from New York three weeks previously. There were many flies about their premises, a horse next door and goats across the street. The patient had been in swimming at South Beach.

Patient 13, another child, gave no history of contact, but eleven days later a waitress (case 15) who had lived in the same apartment house with her became ill with poliomyelitis. The waitress had recently visited in Miami and had swum at South Beach. A son of a steady customer was said to have had poliomyelitis. Fifteen days after patient 13 had the onset of poliomyelitis, a child across the street (case 27) also became ill with the disease, The latter child's father ran a lunchroom.

Whereas 12 of the first 14 patients were children, 6 of the next 7 patients were adults. Patient 15, the wife of a commander aboard another submarine, began to have prodromal symptoms while on a visit to Miami and exhibited acute symptoms eight days after returning to Key West. On the day she was admitted to the hospital, the 17 month old son (case 16) of the executive officer aboard the same submarine was admitted with poliomyelitis. As a matter of fact, the boy (case 16) frequently visited her home. Significantly, no other cases were reported from the families of men aboard this submarine.

Patients 22, 24 and 27 had no known contacts. They had swum at Rest Beach. Each of these patients had chickens on the premises or next door and many flies. Case 23, that of a 2 year old girl, was interesting, since her parents claimed to have isolated her strictly on the day the first case of poliomyelitis was reported

in Key West. She drank boiled milk and water, was allowed no visitors and was not permitted to be outside. The family raised chickens. Garbage cans were sprayed with DDT. Two doors away, however, there was a filthy yard, with many flies.

Patient 25 gave no history of contact. His parents had been in Miami three weeks previously, and he had been to nursery school in the Poinciana area.

Patient 26, an Army private who lived in Poinciana, gave no history of contact. He had been on a fishing party, where every one drank from the same bottle of water. One of his companions on the party subsequently came down with what was thought to be abortive poliomyelitis.

Patients 29, 31 and 32 all became ill about the same time. Patients 29 and 32 were a native boy, aged 3 years, and his mother (in her third trimester of pregnancy). Patient 31 was a near neighbor's son, who visited frequently at her home and who, three weeks previously, had just moved to Key West from Miami.

Patient 30 was a 19 month old baby from Rest Beach who, three weeks before, had moved over from Poinciana.

Patient 33, an officer's wife, was admitted three weeks after delivery. She had been visited in the hospital by the mother of a patient with poliomyelitis about seventeen days prior to admission. It was subsequently known that her husband had a febrile illness, with headache and stiffness of the neck and back for three days, but he did not consult a doctor.

Patient 34, a Wave who lived in the hospital barracks, returned from a fourteen days' leave four days before she became ill. She had been in Miami two days. She had swum at Rest and South Beaches. She had dated the Army physician, who, eleven days previously, had examined and admitted patient 26. Her roommate had the onset of probable abortive poliomyelitis three days after she was admitted. Significantly, this was the only case of typical abortive poliomyelitis seen among members of the hospital staff.

Patient 35, an officer's wife, recently treated for menorrhagia and "influenza," presented acute symptoms on the way to Palm Beach. Her husband daily brought home from work the husbands of patients 20 and 21.

Patient 36, the pregnant wife of a medical officer at the submarine base dispensary, had been in the hospital two weeks previously with an attack of pyelitis. There was no history of contact. She had been swimming at Rest Beach regularly.

Patients 37 and 38, sons of a commanding officer of another submarine, had been strictly isolated at home ever since the epidemic began. They remained at home and were allowed no visitors. However, their parents had been in Miami two weeks before their children exhibited acute symptoms. These children were leaving this area to escape contagion, but became ill with the disease en route to California.

Patient 39, the pregnant wife of an enlisted man, aboard the same submarine as the husbands of patients 5 and 17, gave no history of contact. She became acutely ill one month after the last reported case. She had not been swimming. She had stayed at home and avoided crowds. She had, however, attended a dance three weeks prior to her admission. Garbage and sewage disposal was satisfactory.

Patient 40 was a chief at the submarine base. His wife had had a febrile episode with stiff neck about ten days before. He had been swimming regularly at South Beach twice a week.

From the standpoint of possible incrimination of flies and garbage, it is interesting to study the east to west spread of poliomyelitis in Poinciana, the earliest and largest single area hit (13 cases). There are four groups of dwellings in this area.

To the east is Poinciana Place (a housing project of 210 dwelling units), in the region of which 8 cases developed. Near this project, to the east, there is a stable of horses, goats and poultry, where flies breed in large numbers. The prevailing breeze is from the east or southeast. The first group of cases (2, 3, 4, 6, 8 and 10) came from this area. Adjoining, westward, is Poinciana Extension (a project of 550 dwelling units), where only 1 case (26) developed, three weeks later. Farther west are West Poinciana (with 140 housing units), where the next 2 cases (7 and 9) developed, and the MacArthur Homes, cases 16 and 17 being reported in this and in the adjoining area.

It is noted that the largest housing project (550 units) had the least number of cases (1). On inspection, this project had much fewer flies than did the other areas. For example, no fly larvae were found in Poinciana Extension, while about 25 per cent of the garbage cans in West Poinciana contained fly larvae.

Practically all these units have the same water supply and the same sewage system and receive milk from the same dairy, and the tenants have the same social and financial status, suggesting that these factors were not incriminated in the epidemic.

It is also to be noted that in the two other housing projects, Porter Place (136 units) and Fort Village (158 units), no cases were reported. Their location was far removed from the Poinciana and Rest Beach areas.

At the homes of 15 of the 24 patients not from the Poinciana area, the garbage and fly situation, either on the premises or next door, was described as "bad." Garbage cans often contained many maggots.

Thus, direct contact, flies and the beaches (polluted water) could not be excluded as important factors in the local spread of the disease.

PREDISPOSING FACTORS

The influence of various conditions on the susceptibility to poliomyelitis has been much discussed. It has been claimed, for example, that a recent tonsillectomy may provide an easy path of entry for the virus, predisposing particularly to bulbar involvement. None of the 40 patients in this series had had a tonsillectomy in the past two years. Increased fatigue or excessive exercise is said to be a predisposing factor. Four patients gave a history of recent excessive work or exercise.

It has been noted that people who have poliomyelitis are usually well nourished and healthier than the average. All but 4 of the patients could be considered as well nourished, better than the average. Three had had recent illnesses (patient 36, pyelitis with pregnancy, two weeks previously; patient 35, fever following immunizations, four days previously). One patient was malnourished and had been drinking heavily prior to admission. One patient was recently parturient.

The influence of pregnancy on susceptibility to poliomyelitis is not known.[1] The incidence in this epidemic (6 pregnant and 1 parturient patient, or 17.5 per cent of the series) is the highest ever reported in an epidemic of poliomyelitis. In 1945 Fox and Sennett [2] stated that only 85 cases of the disease in pregnant women had been reported in the literature.

Aycock [3] expressed the belief that the endocrine glands may influence resistence or susceptibility to poliomyelitis. He injected poliomyelitis virus intravenously into castrated female monkeys and into normal controls. Some of the castrated monkeys were prepared by receiving a course of estrogen therapy. He reported that the estrogen-prepared animals showed a significantly increased resistance to poliomyelitis and that in the monkeys which did succumb the onset of the disease was delayed. He also showed that a group of poliomyelitic patients had a higher urinary excretion of estrogens than did the normal controls.

Why, then, do not the higher amounts of estrogen in pregnancy protect the patient? The answer seems to be that the hormonal status of the pregnant woman differs from that of the nonpregnant woman, as well as the castrated animal. While estrogens increase in pregnancy, pregnancy is dominated rather by progesterone (produced by the corpus luteum and by the placenta). Estrogen and progesterone are physiologically antagonistic. Since other normal secretions, such as that of the pituitary gland, are also increased during pregnancy, the end effect of several interacting variables, including increased estrogen, may differ from the effect of increased estrogen alone.

The effect of estrogen may be pronounced, or more unopposed, during the first trimester. This might explain Weaver and Steiner's [4] report that 3 of 13 rats inoculated during the first trimester of pregnancy resisted infection with poliomyelitis virus, whereas all animals inoculated in the second or third trimester, as well as virgin animals, were uniformly susceptible. It might explain the incidence of poliomyelitis in 75 women (cited by Weaver and Steiner [4]) distributed according to trimesters: first trimester, 17.1 per cent; second trimester, 34.3 per cent, and third trimester, 48.6 per cent. Of our series, 1 patient was in the first trimester; 4 were in the second, and 2 were in the third. Was the onset of the disease delayed in the pregnant woman? It is not possible to say. However, 4 were among the last 8 patients to be admitted. The other 3 were admitted in midepidemic. The only case occurring in the first trimester was case 39 (in the ninth week of pregnancy).

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2. Fox, M. J., and Sennett, L.: Am. J. M. Sc. **209**:382, 1945.
3. Aycock, W. L.: Endocrinology **27**:49, 1940.
4. Weaver, H. M., and Steiner, G.: Am. J. Obst. & Gynec. **47**:495, 1944.

A factor common to all the pregnant patients (6 Navy wives and 1 civilian) in this series was their abundant use of vitamin supplements. Five other patients took additional vitamins regularly; 5 did not; for the rest information on this point was not available. This observation is of some interest, since Foster and associates,[5] in experiments with mice maintained at various levels of thiamine intake, reported that the incidence of paralysis for mice given injections of murine poliomyelitis virus (Lansing strain) was several times as high on the high thiamine diet as on the thiamine-deficient diet. Similar observations were made by Rasmussen and associates.[6] In some instances in which thiamine-deficient mice were subsequently given adequate thiamine they became paralyzed after a prolonged incubation period. Partial starvation of the animals on a complete diet also increased the resistance of mice to the virus, but it was demonstrated that the vitamin deficiency exhibited a greater protection than did the restriction of food intake, indicating that the effect of the vitamin deficiency could not be entirely due to inanition. Induced deficiencies of riboflavin, pyridoxine, protein and tryptophan had no effect on the resistance.[7]

Draper [8] described a certain constitutional type of child as susceptible to poliomyelitis. Briefly, children who become ill with poliomyelitis are large for their age; they are all broad faced children, with high cheek bones. Their eyes are wide set. The space between the inner canthi is also wider than normal, so that the whole expression is that of a flat-faced, broad, almost Icelandic type. In addition, there is a definite design of the bony skeleton, especially of the skull and hands. The gonial angle between the posterior border of the ascending ramus and the inferior border of the horizontal ramus of the mandible is wide, and the subcostal angle is narrow. The teeth are large for the size of the face and are usually irregular.

This disease occurs almost entirely in brunets. If one observes the blond patients closely, one will find that they are covered, in many cases literally covered, with deeply pigmented spots. The mothers of many patients with poliomyelitis are thyroid types. The fathers are often of the eunuchoid, giant form of the Fröhlich type. The genital inadequacy of the boys with poliomyelitis is striking.

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5. Foster, C.; Jones, J. H.; Henle, W., and Dorfman, F.: Proc. Soc. Exper. Biol. & Med. **51**:215, 1942; Science **97**:207, 1943; Am. J. M. Sc. **205**:465, 1943; J. Exper. Med. **79**:221, 1944.

6. Rasmussen, A. F., Jr.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: J. Infect. Dis. **74**:41, 1944.

7. Jones, J. H.; Foster, C., and Henle, W.: Am. J. M. Sc. **211**:245, 1946.

8. Draper, G.: Acute Poliomyelitis, Philadelphia, P. Blakiston's Son & Co., 1917.

Patients 16 and 27 fitted Draper's description well. However, the description was of little clinical aid. Five of the patients had blond, or almost blond, hair and fair complexion; 4 others were of fair complexion and had light brown or brown hair.

It has been suggested that some families are constitutionally more predisposed than others to diseases of the nervous system. Surprisingly, 3 of the patients reported the previous incidence of poliomyelitis in their families. The aunt of patient 14 was a victim of poliomyelitis in Key West seven years ago. The nephew of patient 20 and the sister of patient 24 also were said to have had poliomyelitis.

PERIOD OF INCUBATION

About one-half the 40 patients gave a history containing clues to the length of the incubation period. For example, patient 28, who died of bulbar poliomyelitis, had the onset of acute symptoms seventeen days after his wife's (case 19) prodromal symptoms and ten days after she became acutely ill. Patient 19 was admitted with acute symptoms fifteen days later than patient 5, at whose home her children played. Patient 12 had moved to Key West from New York less than three weeks before he became ill. Patient 15 had returned from a week-end visit to Miami ten days before she became ill. Patient 33 was visited, in the hospital after the birth of her baby, by the mother of a patient with poliomyelitis almost three weeks before she became sick.

On the basis of such reasoning, the period of incubation ranged from seven to twenty-two days for this group of patients, with an average of about two weeks. This is about the average usually ascribed to cases of the paralytic type. The range of the incubation period is usually given as five to thirty-five days.[9]

CLINICAL OBSERVATIONS

Symptoms.—Four fifths of the patients had a definite prodromal period of from one to eight days (for 1 patient, three weeks). Oftenest the prodromal period was one to four days and consisted of some of the following symptoms: general malaise, weakness, fever, irritability, fatigue, sore throat, muscular pains, insomnia, headache, dizziness and nausea.

The presenting acute complaint depended on the stage at which the patient was first seen. Three fourths of the civilian patients (mostly children) were first seen in the paralytic stage; hence, a limp or inability to walk was the commonest complaint of these patients, together with

9. Rasmussen, A. F., Jr.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: J. Bact. **45**:85, 1943.

fever and headache. Over one-half the Navy patients (largely adults) were seen in the acute, preparalytic stage. An additional one-fourth were first seen with minimal prodromal complaints, so that the natural course of events in this disease was clearly demonstrated.

The onset of acute symptoms was gradual in 35 patients. The other 5 patients first noted the symptoms on awakening in the morning. The earliest acute symptoms were usually mild fever, headache, sore throat, backache, neck ache, malaise and vomiting. Headache (severe in 4 patients) was the commonest complaint, being recorded for 27 patients. Only 4 patients reported having had no headache. (The 9 other patients were small children.) All but 1 of the adults complained of headache. The duration of headache before admission varied from one to eight days, usually from one to three days.

Malaise, drowsiness, irritability and restlessness were frequent complaints. Only 3 patients claimed not to have these symptoms. Nine patients complained of all four.

The highest temperature before admission was said to be 105 F. The temperature on admission depended partly on the stage at which the person was seen, since the temperature is usually highest in the acute, preparalytic stage. The highest temperature on admission was 104 F.; the average was a little above 101 F. Seven patients had a normal temperature (under 98.6 F. orally, or under 99.6 F. rectally) on admission; the disease of 2 of these was in the preparalytic stage. (After admission the temperature of 1 of these 2 patients rose from 98.4 to 101 F.; that of the other, from 98 to 100 F.) This is an important point in an epidemic. Since fever is usually one of the cardinal signs of an infection,[10] a patient suspected of having poliomyelitis who has no fever, but mild symptoms, may be prematurely dismissed. In a suspected case, it is worth while to inquire routinely about recent fever, although the temperature at the time of examination is normal.

CASE 40.—An enlisted man aged 33 was seen on August 6, complaining of moderate headache and slight stiffness of the neck. Eight days before admission he first began to feel malaise. During the next five days he complained of indigestion, fatigue, absent-mindedness and continued malaise. Three days before admission there developed a severe headache, which went away after an hour and returned the same night, along with fever (which his wife first noted). Two mornings before admission he became nauseated, and his back and neck felt stiff and hurt slightly on flexion. Examination by the dispensary physician was said to have shown nothing abnormal at the time. At the time of admission, at his wife's insistence, his headache, backache and neck ache were gradually disappearing and, except for the mild headache, he was comfortable. He had had no fever in two days. Ten days before his wife had complained of fever and stiffness of the neck.

Examination.—The temperature was 98.4 F., the pulse rate 72 and the respiratory rate 22, per minute. Examination revealed nothing significant except for some

10. Discussion on Aycock, W. L.: A. Research Nerv. & Ment. Dis., Proc. (1931) **12**:114, 1932.

pain in the midback when the patient bent his head between his knees. There was no limitation of action. The reflexes were normal.

Laboratory Data.—The spinal fluid contained 521 white cells (18 polymorphonuclear leukocytes and 503 lymphocytes). The white blood cell count was 6,000, with 46 per cent polymorphonuclear leukocytes and 54 lymphocytes. The sedimentation rate was 6 mm. in one hour (Westergren method).

Course in Hospital.—The day after his admission the patient's headache almost completely disappeared. He has been asymptomatic except for mild malaise. He is limber, and no subsequent weakness or paralysis has developed (this case is the second nonparalytic one in the present series).

The patient may give no history of fever, despite its presence. Patient 21, a woman aged 23, had a temperature of 101.8 F., and patient 10, aged 14, a temperature of 102 F., on admission; yet neither had experienced the sensation of fever.

In this series, fever was present from one to twenty-one days before admission, usually from one to three days. There were 9 instances of recurrent fever (two episodes). The duration of fever was from no to nine days after admission, with an average of about four days. Five children had a low grade "fever" throughout their three weeks or more in the hospital (up to 100 or 100.6 F. daily, rectally).

The highest temperature was 107.6 F. (rectal), recorded in the case of patient 26, who died of the ascending Landry type of spinobulbar poliomyelitis, seven days after admission.

Only 4 patients noted chills. Sore throat, occasionally severe, occurred in at least 18 patients. Fifteen patients (including 4 of the 6 pregnant women) complained of nausea and vomiting; 8 other patients experienced only nausea. Only 2 of the 40 patients had definite diarrhea, but 3 others reported loose or slightly increased bowel movements. Seven patients complained of constipation. All but 2 of the patients gave a history of slight to moderate neck ache and backache and stiffness prior to admission. Five children complained of abdominal pain. Dysphagia was present initially in 4 patients; regurgitation of fluids, in 2; dysuria or oliguria, in 4 (not including the pregnant women); aphonia or dysphonia, in 2, and tremors, in 3. Fourteen patients complained of stiffness or pain in muscles other than those of the neck and back.

Other Physical Findings on Admission.—The pulse rate was under 90 per minute for 25 of the patients and rose as high as 160 and 178, respectively, for 2 of the other (adult) patients. The respiratory rate was usually normal. Stiffness of the neck and back was usually present, varying from slight to extreme. Three of the patients had no stiffness or pain on motion of the neck and back at any time. The stiffness was usually much less than that encountered with meningitis. Kernig and Brudzinski signs were noted in only 7 patients. Eight patients (3 small

children and 5 adults) had only slight stiffness, which, particularly in small children, might have been overlooked by the inexperienced examiner. Indeed, early in the epidemic, the Foundation's physiatrist demonstrated stiffness of the muscles of the back of a month old baby which was entirely missed by the medical officer, who had not been in an epidemic of poliomyelitis before.

Sixteen of the patients had mild to severe pharyngitis. For 3 the pharyngitis was pronounced and dominated the clinical picture on admission. A mild degree of associated cervical lymphadenopathy was noted in only 4 patients. Six patients had prominent respiratory signs, including dyspnea, tachypnea, respiratory splinting and abdominal breathing. Two thirds of the patients exhibited weakness or paralysis (of the extremities, vocal cords, muscles of swallowing or muscles of respiration) on admission. In the small children, of course, partial weakness was sometimes difficult to demonstrate.

Reflex changes were only occasionally of value in making an early diagnosis or in predicting the site of involvement. In 11 patients the reflexes were entirely normal on admission. Four others had generally hyperactive reflexes. When the reflexes were hyperactive, they were more often bilateral than unilateral. Unilateral diminution or increase in reflexes was occasionally of aid in the early detection of muscular weakness. In the preparalytic stage, the reflexes in an involved limb were usually at first hyperactive, later becoming diminished or absent. The abdominal reflexes and the knee jerks showed the most frequent changes (24 patients).

In 18 patients hyperirritability and tremulousness were prominent. Four of the patients had definite tremors and involuntary grimacing. Intense hyperesthesia was noted in 2 patients.

COURSE

The length of the acute stage was usually from three to ten days. The end of the acute stage was defined as the time at which the progression of paralysis or acute symptoms had ended and the elevation of temperature and other signs due to the poliomyelitis had subsided, with return to or toward normal.

The period between the onset of acute symptoms and that of paralysis was from one to three days for all but 5 of the patients: For 1 of the latter it was eight days; for another, twenty-four days.

The number of days of progression of the paralysis was usually from one to three (with an average of two days). Only in 1 case was it definitely longer than four days.

CASE 31.—A 7 year old white boy was admitted to the hospital on June 30 with headache, fever and aphonia. His illness had begun three days previously with the onset of fever. Headache, fever (temperature, 100 to 102 F.) and drowsi-

ness continued until his admission. Eighteen hours before admission he became unable to talk and had slight dysphagia. There were no other symptoms.

Related History.—The patient had moved to Key West from Miami three weeks before onset of the present illness. Two persons in close contact with the boy (patients 29 and 32) had poliomyelitis. The family used a septic tank. At the neighboring house "ripe" garbage with heavy breeding of flies was found.

Physical Examination on Admission.—The temperature was 103 F., the pulse rate 120 and the respiratory rate 45. The blood pressure was 120 systolic and 70 diastolic. The patient was well developed and well nourished. He was in a semicomatose state and breathed abdominally. There was no stiffness of the neck or back. The reflexes were not recorded.

Laboratory Data.—The spinal fluid contained 31 white cells (3 polymorphonuclear leukocytes and 28 lymphocytes). The protein content was 15 mg. per hundred cubic centimeters. The white blood cell count was 8,600, with 63 per cent polymorphonuclear leukocytes, 35 lymphocytes and 2 per cent eosinophils. The urine showed a slight trace of albumin.

Course in the Hospital.—The patient remained semicomatose during the first twenty-four hours but was able to void and take a few sips of fluid by mouth. His nail beds were slightly cyanotic. The next day his temperature dropped to 100 F. and he appeared more responsive. The following day his color and dysphagia improved and he responded to questions. He steadily improved and was able to stand, with uncertain balance, on July 4 (four days after his admission). The next day muscular evaluation showed no obvious weakness. On July 10 he complained of soreness in the back and pain in the hamstring muscles of the right leg on walking. Spasm was present in this group of muscles, as well as in the right calf. The next day there was no pain, but the muscles of the hamstring group were weak. During the next three days he walked with a limp, but with hot packs, whirlpool baths and passive exercises the affected limb rapidly improved, and by July 18 it was entirely normal again. He exhibited no residual sign and was discharged on July 20.

MUSCULAR INVOLVEMENT

Paralysis of various muscle groups was transient in 4 patients (two days to two weeks). In 6 other patients weakness apparently disappeared after a month. Five patients had no apparent paralysis. In the remaining 22 patients paralysis is still present.

Ten patients had transient or prolonged bulbar involvement of one or both upper extremities in the earlier part of the epidemic. There were 3 deaths among the 8 patients who had had bulbar involvement for more than twenty-four hours, a mortality of 37.5 per cent. Death occurred one, three and five days after admission, respectively. In the earlier part of the epidemic, 6 of the first 11 paralytic patients had involvement of the left upper extremity alone. None of the patients since that time had involvement of the left upper extremity alone. The average number of extremities involved in cases of transient or prolonged paralysis was two (1.9 per cent).

Four patients had involvement of all four extremities. Patient 26 had acute ascending and descending paralysis, ending in death.

CASE 26.—An army private aged 19 was admitted on June 19, complaining of sore throat, fever, headache and malaise. He had been well until seven days before admission, when he felt ill, was lethargic and experienced moderately severe headache. These symptoms had continued. Two days before admission he began to have sore throat and fever. His neck and back became moderately stiff and uncomfortable. The patient's sister had had poliomyelitis four years previously.

Physical Examination on Admission.—The temperature was 100 F., the pulse rate 104 and the respiratory rate 28, per minute. The blood pressure was 120 systolic and 76 diastolic. Examination revealed moderate rigidity of the neck and, to a less extent, of the back. There was bilateral tightness of the muscles of the hamstring group. The reflexes were generally hyperactive. There was a general feeling of weakness but no muscular weakness.

Laboratory Data.—The spinal fluid (June 19) contained 179 white cells, with 31 polymorphonuclear leukocytes and 148 lymphocytes. The protein content was 50 mg. per hundred cubic centimeters. On June 23 the cell count of the fluid was 230, with 2 polymorphonuclear leukocytes and 228 lymphocytes.

Course in Hospital.—The next morning, June 20, the stiffness of the neck and back had become more pronounced, and weakness of the right arm had developed. The patient began to vomit frequently. He complained of difficulty in swallowing and inability to take a deep breath. His right arm became limp on June 21, and he had pronounced dysphonia and dysphagia. Respirations were irregular. He obtained little relief from increasing dyspnea in an oxygen tent. His left arm became flaccid. He complained of pain in the chest and throat and was unable to take a deep breath. His respirations became more regular, and he was placed in a respirator (with oxygen), with much relief. His color was mildly cyanotic, however. Constant suction had been employed and atropine administered for removal of mucus. He began to have difficulty in moving his legs and was unable to void. The next day, June 22, his temperature rose from 98 to 104 F., and he became semicomatose. He became unable to move his legs or arms. He had been given penicillin therapy as a prophylactic measure. His color was constantly cyanotic. On June 23, he still brought up some mucus, had great difficulty in breathing (even in the respirator) and became comatose. Spinal puncture was performed, with the patient in the respirator. Treatment was continued with oxygen, suction, fluids, enemas and catheterization. He died the next day.

Case 15 is an example of the acute ascending Landry type, which stopped just short of the medulla (transient facial paralysis, dysphagia and dysphonia). The patient has now been two months in an "iron lung," with nearly complete flaccidity of all four extremities and involvement of the muscles of respiration. Her paralysis was complete within twenty-four hours after it began.

Inability to void was present from one to two days in 4 patients, three days in 1 patient and from six to seven days in 4 patients. The last 5 patients included 4 of the pregnant women and the 1 parturient patient.

LABORATORY DATA

Spinal Fluid.—The number of cells in the spinal fluid bore no relation to the severity of the disease, and was only roughly correlated with the clinical degree of meningeal "irritation." For example, patient 21,

who had only slight stiffness of the back and neck, had 428 cells per cubic millimeter and only mild involvement of the lower extremity. Patient 40, who had only slight discomfort in the midback on bending, had 521 cells per cubic millimeter of the spinal fluid and no weakness or paralysis. Patient 24 had a rigid, "poker" back and 171 cells but had never experienced any weakness.

After a great number of examinations of the spinal fluid of persons who were suspected of having the disease but who had almost minimal symptoms and signs (for example, a member of the patient's family), it became apparent that in the absence of signs of meningeal "irritation" the spinal fluid would be normal, even if the history was suggestive of the disease. However, careful watchfulness for slight meningeal changes was necessary.

CASE 34.—A Wave had questionable stiffness of the neck and back when she was first seen. She was not sure that she had had any fever (98.8 F.). Because of a headache of three days' duration and aching in the shoulder muscles, she was admitted for observation, and a spinal puncture was performed. The fluid contained no white cells; the protein content was 15 mg. per hundred cubic centimeters. Nine hours later there were definite stiffness in the lower part of the back, discomfort on flexion of the neck and hyperactive abdominal reflexes. Spinal puncture at that time revealed 23 white cells per cubic millimeter, all of which were lymphocytes. Three days later weakness developed in the right lower extremity.

In the series of 40 patients, the cell count of the spinal fluid varied from a low of zero (3 cells per cubic millimeter on repeated taps) to a high of 563 per cubic millimeter. Six patients had over 400 cells per cubic millimeter, the average being 151 cells. This value is higher than the usual range given for poliomyelitis (15 to 150 cells per cubic millimeter). Seventeen, or less than one-half, had less than 100 white cells per cubic millimeter; only 1 patient had less than 10 cells.

Merritt and Fremont-Smith [11] found that the highest white cell count occurs in the preparalytic stage, with the cells predominantly of the polymorphonuclear type. After the onset of paralysis there is sooner or later a shift toward a predominance of lymphocytes. The present findings are in agreement. All but 2 of the patients in the preparalytic stage (on admission) showed predominance of polymorphonuclear cells. In addition, one third of the paralytic patients showed predominance of polymorphonuclear leukocytes. Three patients had 97 per cent or more polymorphonuclear cells (97 per cent of 405 cells, 97 per cent of 428 cells and 98 per cent of 171 cells, per cubic millimeter). Two others had over 90 per cent polymorphonuclear cells. The fact that many of these patients were seen unusually early in the course of the disease and were followed closely may account for the observation of a high per-

11. Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B Saunders Company, 1937, p. 130.

centage of polymorphonuclear cells. Repeated examinations of the spinal fluid were not made routinely.

The protein values were of interest. Eight of the 10 patients sent to Jackson Memorial Hospital had elevated protein levels (over 40 to 45 mg. per hundred cubic centimeters). However, only 2 of the other patients had an increased protein content of the spinal fluid. This result may have been due to use of a faulty reagent.

The sugar and chloride levels were normal, and no organisms were cultured from the spinal fluid in any case.

Blood.—Slightly over one-half the patients had a normal blood count; the remainder had a mild leukocytosis. Only 3 patients had a white cell count of over 12,000, 2 of these having the bulbar form of the disease. The highest count, 17,400, was that of a child who also had an acute streptococcic throat. The differential count was usually normal. Four children had a relative lymphocytosis, the number of lymphocytes varying from 63 to 78 per cent. No atypical lymphocytes were seen.

DIFFERENTIAL DIAGNOSIS

There were few problems in differential diagnosis. Conditions to be differentiated from poliomyelitis were acute pharyngitis, gastroenteritis, torticollis, septicemia, infectious mononucleosis, meningitis, pregnancy and hysteria.

CASE A-5.—An enlisted man aged 24 was admitted on June 28 for observation for suspected poliomyelitis, with the complaint of backache of one day's duration. After lunch he had noticed weakness and dizziness on bending over. In the afternoon a slight headache appeared, and the patient began to have moderate discomfort and slight stiffness in the small of his back; in the evening he became feverish, and his legs began to feel weak. The related history was without significance. One of his close friends had recently been suspected of having poliomyelitis.

Physical Examination.—The temperature was 101.6 F., the pulse rate 82, and the respiratory rate 21. Examination revealed nothing significant except for slight stiffness and discomfort of the lumbar region. The reflexes were normal.

Spinal Fluid.—The spinal fluid contained 1 white cell (lymphocyte) per cubic millimeter and 15 mg. of protein per hundred cubic centimeters.

Course in Hospital.—On June 29 his shoulder muscles ached and his headache increased. There was increased stiffness in the lower part of the back, which continued the next day. On July 1, the aching in the shoulder had abated, but the patient still had mild generalized headache. On second examination the spinal fluid was normal (no white cells, 10 mg. of protein per hundred cubic centimeters). The temperature was normal at this time, and the patient felt that he was ready for duty on July 2. On standing, however, his headache and backache returned, and he was kept in the hospital until July 6 before being discharged.

Impression.—The diagnosis was that of possible abortive poliomyelitis.

CASE A-1.—A Wave, aged 21, whose roommate had been admitted with a diagnosis of poliomyelitis four days previously, was first seen on the night before her admission, complaining of headache. The generalized headache had begun on June

30, while the patient was working in the family clinic. It had persisted unabated. Except for a general feeling of tiredness, the patient had no other symptoms until the day before admission. On the morning of July 4 she began to notice aching in her neck and the upper part of her back. She had no fever. She was examined that night, when, except for slight stiffness and tenderness (and accentuation of headache) on bending of the neck, there were no positive findings. The reflexes were normal, and there was no evidence of muscular weakness or spasm. The next morning, July 5, the day of admission, the patient was unable to get out of bed. Her neck and the upper part of her back were stiff, and her headache was severe. She had no fever.

Physical Examination on Admission.—The temperature was 98.6 F., the respiratory rate 20 and the pulse rate 84. The patient, who was well developed and well nourished, appeared acutely ill. Physical examination revealed nothing of significance except severe stiffness and pain in the neck and back. The headache was intense. The reflexes were normal. There was no evidence of muscular weakness. The patient appeared somewhat generally weak. She could not sit up.

Spinal Fluid.—The cell count was zero; the total protein content, 15 mg. per hundred cubic centimeters.

Course in Hospital.—During the patient's first day in the hospital her neck and back grew stiffer and she became increasingly uncomfortable. Repeated examinations of the spinal fluid revealed a normal picture (2 lymphocytes per cubic millimeter and 10 mg. of protein per hundred cubic centimeters). That night her symptoms reached their peak; and from July 7 until her discharge, on July 12, there were gradual recession of the neck ache, backache and stiffness and gradual diminution of the headache. For three or four days, however, she had severe headache and neck ache on standing for more than a few minutes. Throughout her stay in the hospital her temperature remained normal, and she gave no evidence of muscular weakness at any time.

Impression.—The diagnosis was probable abortive poliomyelitis.

Case A-8.—A boy aged 4½ years was admitted for observation on July 12, complaining of pain and stiffnes in the left leg, which caused him to limp. About June 5 he had spent three days in bed with fever (temperature, 102 to 103 F.), sore throat and headache. About June 15 he began to feel dizzy and "dopey," and his legs were weak. These symptoms lasted two weeks. Three days after the initial symptoms the left leg and thigh began to hurt and to tire easily. From that time until his admission he complained of pain and stiffness in his left leg. On the day before admission a definite limp developed. He had no stiffness of the neck or back. There was no further fever. Examination revealed a normal status except for pronounced spasm of the hamstring muscles and around the hip on the left side. He improved rapidly under treatment with whirlpool baths and was allowed to go home after three days. No examination of the spinal fluid was made. He limped again at home for two days or so and then seemed well. He complained of occasional stiffness in the left thigh, but on subsequent weekly examinations no weakness was demonstrated.

Case A-9.—The mother of the boy in case A-8 also gave a history of a febrile episode at the time of her son's. She also had a slight limp about the same time that he did, but on the right side. She had had fever, headache and slight nuchal discomfort, but no definite stiffness or pain in the neck or back. She was examined by the physiatrist, who could demonstrate no definite weakness or spasm. After a few days her limp ceased.

Impression.—The diagnosis was possible abortive poliomyelitis.

CASE 8-A.—A white woman aged 22, the mother of a patient with poliomyelitis, was admitted to the hospital on July 4, with the clinical diagnosis of poliomyelitis, made by her family physician. She complained of aching and stiffness of the neck and back, sore throat and weakness of the right arm and leg. She had been well until June 28, when her menstrual period began. During this monthly period and the preceding one there had been profuse menorrhagia. She had used at least twenty-four pads a day and was so weak that she stayed in bed most of the time. (Her periods were regular and usually lasted ten days.) While in bed, a week before her admission, and one week after her son was admitted with poliomyelitis, she noticed a low grade fever (temperature 99 to 100 F.), headache (chiefly occipital) and persistent drowsiness, hyperirritability, restlessness and malaise. Two days before her admission, a sore throat developed which continued until her entrance to the hosptial; on the same day her right leg became weak (she noticed this when she walked across the room). The day before her admission her neck and back became increasingly stiff and ached. Her right arm and leg ached, and both became weak (the leg being the weaker). She vomited once and complained (in answer to questioning) of dysphagia and some regurgitation of fluids. Her headache was still present, and she said her temperature was 100 F. on the day before admission. On admission, she appeared rather weak, and was still menstruating.

Laboratory Data.—The spinal fluid was colorless, with no cells and a protein level of 10 mg. per hundred cubic centimeters. The white cell count was 9,200, with 58 per cent polymorphonuclear leukocytes (32 segmented and 26 nonsegmented forms), 36 per cent lymphocytes, 3 per cent eosinophils, 2 per cent basophils and 1 per cent monocyte. The red cell count was 3,900,000, with a hemoglobin concentration of 80 per cent. The urine was normal. The sedimentation rate was 8 mm. in one hour (Westergren method).

Physical Examination on Admission.—The temperature was 100 F., the pulse rate 80 and the respiratory rate 20, per minute. The blood pressure was 100 systolic and 70 diastolic. The patient had a washed-out appearance and seemed to be in considerable pain and discomfort. She held her neck and back stiff and complained of considerable tenderness on motion. There was apparent weakness of both the right arm and the right leg. The physiatrist noted muscular spasm in the right shoulder girdle and the right hip. All the reflexes were normal. The patient spoke in a very weak voice. She lay quite still.

Course in Hospital and Treatment.—After physical examination and studies of the spinal fluid, the patient was admitted to the hospital for observation. Two hours after her admission the physician on call was summoned because the patient began to have "muscle spasms" in her hands and arms and numbness and "drawing" of both hands. The patient exhibited a typical hyperventilation syndrome. There were bilateral carpal spasm and some laryngeal spasm, and the patient (as the hyperventilation increased) complained of severe dyspnea, dysphonia and dysphagia. Rapid intravenous administration of calcium gluconate stopped the hyperventilation. Then, sodium amytal, 7½ grains (0.49 Gm.) was given slowly intravenously. The patient became clinically intoxicated; she then readily got up and walked about, without a trace of weakness or stiffness, and began joking with the physician. At no time after the amytal session did she exhibit any evidence of tenderness or stiffness in the neck, back or other muscles. She had no further complaints and returned home feeling quite well, after four days.

Impression.—The diagnosis was hysteria and possible mild abortive poliomyelitis.

COMPLICATIONS

Two children (1 in Jackson Memorial Hospital and the other in Key West) had complicating chickenpox. One of the pregnant women with a history of pyelitis had two further episodes of the infection, the last one being complicated with septicemia (E. coli). This condition responded to sulfadiazine.

Poliomyelitis had apparently no effect on any of the pregnancies.

TREATMENT

The treatment in general was that followed by the Georgia Warm Springs Foundation. Special instructions were given the nursing staff with respect to general nursing care; use of hot packs, baths and passive motion; reeducation of muscles, and prolonged observation and treatment after the acute stage of the disease.

SUMMARY AND CONCLUSIONS

1. The clinical and epidemiologic study of an epidemic of 40 verified cases of poliomyelitis and 190 cases of suspected and probable abortive poliomyelitis on the island of Key West is presented.

2. The largest number of pregnant patients (7) reported in any epidemic occurred here. Six had the paralytic form. The possible influence of the endocrine glands and the vitamins is noted.

3. An unusually high number (73.7 per cent) of patients in Navy families were adults (19 to 33 years of age), whereas only 10.5 per cent of the civilian patients were adults.

4. There were 3 instances in which 2 verified cases occurred in the same family (6 patients). Thirteen of the remaining 34 patients gave a history of a febrile illness resembling poliomyelitis in one or more of the family at the same time.

5. Eight patients had a normal temperature on admission. In an epidemic, this is a point worth emphasizing. Since fever is usually a cardinal sign of infection, a patient suspected of having poliomyelitis who has no fever, but mild symptoms, may be prematurely dismissed. It is important, then, to inquire routinely about recent fever or to watch for the subsequent development of fever.

6. In this epidemic a history of direct contact with persons known to have poliomyelitis was obtained for 18 (almost one half) of the patients. Polluted beach water and flies were also possibly incriminated in the transmission of the virus. Three children, said by their parents to have been completely isolated since the onset of the epidemic, had the disease. One patient was visited by the mother of a patient with acute poliomyelitis seventeen days prior to development of symptoms.

Abstracts from Current Literature

Physiology and Biochemistry

SOME NEUROLOGICAL SIGNS AND SYMPTOMS PRODUCED BY CENTRIFUGAL FORCE IN MAN. W. R. FRANKS, W. K. KERR and B. ROSE, J. Physiol. **104**:10P, 1945.

The authors made an extensive study of the neurologic effects of centrifugal force in man on 532 subjects in the human centrifuge with forces varying from 2 to 10 *G*. The reaction times for manual responses to visual and auditory stimuli were recorded, but were not significantly increased except for visual stimuli immediately before black-out. Convulsions frequently occurred, usually after loss of consciousness. These were usually slight, but in a few cases severe generalized convulsions were observed. A number of slight convulsions were noted in fully conscious subjects. Conjugate movements of the head and eyes to one side were sometimes observed. Dreams were frequently experienced. Paresthesias, confused state, amnesia or gustatory sensations were noted with black-out. Incontinence was never observed. Convulsions started during the phase of recovery of the circulatory changes but could not be correlated with any of the measured characteristics of the subjects. Electroencephalograms during increased *G* in conscious subjects showed high frequency, low amplitude waves replacing the normal alpha waves. With onset of unconsciousness progressively slower waves of high amplitude usually appeared. The pattern was not altered by convulsions. THOMAS, Philadelphia.

THE EFFECT OF DIET ON FOETAL DEVELOPMENT. L. R. WALLACE, J. Physiol. **104**:34P, 1946.

An investigation was conducted to decide the effect of maternal diet on the various component parts of the fetus. By feeding ewes on a much restricted ration during the last eight weeks of pregnancy, 144 day old fetuses were obtained whose mean weight averaged only 57 per cent of that of fetuses obtained from liberally fed ewes. Fetuses were also obtained at the ninety-first day of pregnancy, when the experimental treatments commenced. The data resulting from the dissection of these groups of fetuses were compared with the data for fetuses from well fed ewes at twenty-eight day intervals from service.

The results showed that under conditions of restricted nutrition nerve tissue competed for available nutrients more effectively than bone, and bone more effectively than flesh (muscle and fat). Growth of nerve tissue and bone was not depressed as much as that of the fetus as a whole, but growth of flesh more so. The alimentary tract was less affected than the heart; the heart, less than the lungs and kidneys, and the latter, in turn, less than the thymus, spleen and liver.

Wallace concludes that the manner in which the weight increment made by the fetus during any particular period is distributed among the component parts of the body will depend on the extent to which the nutritive conditions then prevailing are limiting the rate of growth of the fetus. THOMAS, Philadelphia.

EXPERIMENTS ON THE HYPOTHALAMIC-PITUITARY CONTROL OF WATER EXCRETION IN DOGS. MARY PICKFORD and A. E. RITCHIE, J. Physiol. **104**:105, 1945.

The daily urinary excretion of water and the immediate diuretic response to the administration of water and isotonic solution of sodium chloride (0.9 per cent) were

observed in dogs before and after the following operations: (*a*) removal of the posterior lobe of the hypophysis alone; (*b*) section of the supraoptic tracts; (*c*) attempted removal of the anterior lobe alone; (*d*) simple hypophysectomy, i. e., removal of the posterior and the anterior lobe at the same time and some of the stalk; (*e*) simple hypophysectomy and section of the supraoptic tracts at the same time.

After any operation involving loss of the anterior lobe the diuretic response to water was diminished as compared with the normal. The creatinine and urea clearances also fell. The diuretic response to the administration of isotonic solution of sodium chloride tended to be greater than the response to the administration of water. The blood pressure remained normal. Denervation of the kidneys did not affect the appearance of the changes mentioned. Dried thyroid, extracts of the anterior lobe of the pituitary gland and of the adrenal cortex and desoxycorticosterone acetate were not found to restore the diminished water diuresis or the lowered renal clearances to normal.

After section of the supraoptic tracts or removal of the posterior lobe alone water diuresis was normal or increased. The average creatinine clearances lay in the normal range. The diuretic response to the administration of isotonic solution of sodium chloride was greater than before operation.

Polyuria may follow any of these operations, even in the absence of the anterior lobe, but only after section of the supraoptic tracts was it of fairly long duration.

THOMAS, Philadelphia.

Diseases of the Brain

NEUROLOGICAL EXPERIENCES IN THE MIDDLE EAST AND INDIA. DOUGLAS MCALPINE, Proc. Roy. Soc. Med. **39**:169 (Feb.) 1946.

Infections of the central and peripheral nervous systems were the main concern of the neurologist in the British armed forces in the Middle East and India. Meningococcic meningitis, practically confined to Indian and African troops, was laid to overcrowding and malnutrition during the winter months. The decrease in mortality from 15 per cent, in early 1943, to 6.6 per cent, in early 1945, and an even greater drop in the incidence of the disease, resulted, according to McAlpine, from the earlier diagnosis and hospitalization, a better standard of medical care and the use of "sulfamezathine" (the dimethyl derivative of sulfadiazine).

Acute benign lymphocytic meningitis occurred in the spring and summer months and was characterized by malaise, fever (averaging five days in duration), headache, vomiting and a considerable degree of prostration. There was variable nuchal rigidity; Kernig's sign was not usually elicited, and the deep reflexes were normal or depressed. The cell count of the cerebrospinal fluid was 20 to several hundred lymphocytes per cubic millimeter predominating, with a return to normal within three weeks.

Tick-borne relapsing fever was frequently complicated by infection of the nervous system. Of 84 cases with neurologic signs, the author observed meningitis in 95 per cent, with the cerebrospinal fluid characterized by pleocytosis, increased protein, often a positive Wassermann reaction and/or a gold curve characteristic of dementia paralytica. Meningoencephalitis was found in 28 per cent; facial palsy, in 21 per cent (bilateral in 4 cases), and papilledema, in 13 per cent. The prognosis with regard to neurologic sequelae was favorable. Arsenical treatment gave disappointing results.

Acute poliomyelitis was described as being commoner than in the British Isles but was rare among the Indian troops. The mortality rate ranged from 18 to over 30 per cent. Prodromal symptoms were roughly divisible into influenzal, catarrhal and gastrointestinal forms. The commonest site of localization was the lower dorsal and lumbosacral portions of the cord. Approximately 50 per cent of the patients had varying degrees of urinary retention. Fatal cases were of the ascending cervicobulbar or bulbar type. Persistent pain in the paralyzed limb was a frequent occurrence. In approximately 5 per cent of the cases the cerebrospinal fluid was normal during either the meningitic or the paralytic phase.

Polyneuritis, either diphtheritic (exceedingly rare among native troops) or nutritional, was frequently observed. The diphtheritic form, commoner in the Middle East, was considered a complication of the cutaneous form of the disease in about one third of the cases. Nutritional polyneuritis complicated typhoid and, to a greater degree, typhus.

One of the principal medical causes of death in India was heat stroke, with several survivors showing permanent sequelae. After recovery from coma, progressive improvement occurred except in a small percentage of cases, in which some signs of dementia remained. Among neurologic sequelae, cerebellar signs were found in several patients.

BERRY, Philadelphia.

OBSCURE NEUROPATHY IN THE MIDDLE EAST: REPORT ON ONE HUNDRED AND TWELVE CASES IN PRISONERS-OF-WAR. J. D. SPILLANE and G. I. SCOTT, Lancet **2**:261 (Sept. 1) 1945.

Spillane and Scott report their observations on a neurologic syndrome which they noted among German prisoners of war. The syndrome, of which they found 112 cases, consisted of retrobulbar neuritis, nerve deafness and ataxic paraplegia, but in many cases only the visual manifestations developed. The illness usually began with failing vision. In some cases this was acute, but in the majority it developed over a period of months. Tinnitus and gradual onset of bilateral deafness frequently accompanied the loss of vision, but in several cases they appeared weeks or months later. Paresthesias of the lower limbs constituted another characteristic complaint in many cases, and in some instances it heralded the onset of disturbances of gait and station. In some cases gross attacks of ataxic paraplegia occurred. There were other occasional neurologic signs, such as trigeminal hypesthesia, loss of taste and smell and partial paresis of the vocal cords. The illness was afebrile, chronic and, in many cases, progressive.

The syndrome was observed almost entirely in a particular camp, the inmates of which had previously been exposed to dietetic deprivations and in which pellagra, dysentery and diarrhea had at one time been prevalent. The authors state the belief that the patients were suffering from a nutritional neuropathy. They are unable to explain why the central nervous system was mainly attacked, in the absence of the common manifestations of nutritional deficiency among the patients affected. Patients who were given intensive treatment with the vitamin B complex responded poorly, or not at all. The results of dietetic therapy were also inconclusive.

YASKIN, Camden, N. J.

SUDDEN APPEARANCE OF PARKINSONIAN SYNDROME AFTER BURIAL UNDER BOMBARDMENT RUINS. M. D. DÉNÉCHAU, Rev. neurol. **77**:80 (March-April) 1945.

Dénéchau reports the sudden appearance of parkinsonism in a man of 33 after burial under ruins during a bombing. The patient had had encephalitis lethargica twenty years previously. He was admitted to the hospital on Oct. 16, 1944 for

tremor of the left upper extremity and difficulty in memory and thinking. He had been active and apparently normal up to June 7, 1944, when he was buried under the ruins of a house during the course of a bombing attack. There was no loss of consciousness or serious injury to any part of the body. When removed from the ruins, he had generalized tremulousness and inability to walk to a hotel 200 meters away without being supported. He remained in this state about fifteen days. The generalized tremulousness then gradually disappeared, and tremor of the left upper extremity was noted. The patient found it difficult to work; he exhibited some sexual erethism and change in character and suffered from headache and somnolence. Neurologic examination showed typical parkinsonism, with fixed facies and loss of associated movements; a cogwheel phenomenon was present in the left upper limb. There was a history of cranial trauma at the age of 2 years and of severe chorea at the age of 7. Careful anamnestic studies revealed that for a few months before the bombing incident the patient had been aware of awkwardness of the left upper extremity. The author apparently believes that the accident transformed a latent or subclinical parkinsonism into the full blown form.

N. Savitsky, New York.

Trauma and Neurosyphilis. J. M. Taques Bittencourt and H. M. Canelas, Arq. neuro-psiquiat. São Paulo **3**:347 (Dec.) 1945.

In addition to an exhaustive review of the literature on the relation of trauma and neurosyphilis, Taques Bittencourt and Canelas report their experiences with 13 personally observed cases—3 of vascular and 10 of parenchymatous neurosyphilis. They conclude that trauma may aggravate preexisting neurosyphilis, precipitate latent or asymptomatic neurosyphilis and be a cause of localization of syphilis in the nervous system even when it is not involved prior to the trauma. They report for the first time 2 cases in which the spinal fluid gave negative reactions immediately after trauma and positive reactions later. The authors conclude that when the intercalary period between the trauma and the onset of the neurosyphilis is between one and six months a causal relation to the trauma is probable; when the interval is six to thirty months the relation to the trauma is more probable, and when the interval is longer than thirty months the relation to the trauma is least probable. While the presence of bridging symptoms between the time of the trauma and the onset of the neurosyphilis is desirable for the establishment of a causal relation, it is not a *sine qua non*. The authors conclude that trauma causes neurosyphilis as a result of significant alterations in the hematoencephalic barrier without gross vascular lesions by altering tissue immunity in the nervous system and by creating tissue changes which are favorable to the growth of spirochetes.

N. Savitsky, New York.

Venezuelan Equine Meningoencephalitis in Man. H. R. Rugiero, A. S. Parodi and A. C. Saenz, Prensa med. argent. **33**:636 (March 22) 1946.

The authors report 8 cases of equine meningoencephalitis in man, all the patients being infected in the same laboratory. Four cases were studied only clinically. In 2 cases the presence of the virus was proved serologically. The serum of patients in convalescence was mixed with the virus and then injected intraperitoneally into rats. In 2 cases the virus was demonstrated directly. In 1 case the clinical picture was very severe, with paralysis of all the limbs, somnolence, violent headaches, fever and delirium. In another case there were two bouts of hyperpyrexia, separated by an afebrile period of two days. The clinical picture in the other cases was that of grip, of greater or less severity—severe headache, diffuse aching, intense myalgia

and backache. Cutaneous hyperesthesia was present in 1 case. There was nothing about the clinical picture to distinguish it from that of other virus-infections. The intensity of antibody formation bore no relation to the severity of the acute infection.

N. SAVITSKY, New York.

DEMENTIA OF THALAMIC ORIGIN. E. GRÜNTHAL, Monatschr. f. Psychiat. u. Neurol. **106**:114. 1942.

Grünthal reports a case in which progressive mental deterioration was associated with disease of the thalamus. The patient, a woman, had always been mentally deficient. She was married and had 3 children, who were said to be feebleminded. However, she had been well adjusted until the age of 35, when gradual mental changes were noted. She began to have difficulty in managing her household affairs. At times she squandered money, and at other times she was excessively penurious. She became noisy, quarrelsome and forgetful and displayed erotic tendencies. These symptoms grew more pronounced, and she was hospitalized at the age of 41. At the hospital she had episodes of aggressive, noisy and fearful behavior, alternating with periods of underactivity and euphoria. She was often confused at night. She misidentified people and had auditory hallucinations. She presented labile emotional reactions, particularly childish laughter, which quickly changed to outbursts of rage. Serologic examination of the blood and the spinal fluid gave negative reactions. The patient's memory became defective, and there was gradually increasing mental deterioration. Fourteen years after her admission she was described as severely demented, out of contact and extremely apathetic. Three years later constant choreic movements developed bilaterally. Death occurred at the age of 60, with signs of bronchopneumonia.

Anatomic examination revealed that the cerebral cortex and white matter were normal, although the brain was small. The thalamus and the red nucleus showed severe alterations, which were bilateral and symmetric. In the thalamus, the changes were confined to the nucleus medialis dorsalis, the nucleus lateralis anterior and the anterior portion of the nucleus lateralis principalis. Most of the nerve cells had disappeared from these areas, and there was a pronounced increase in neuroglia, with perivascular accentuation of the process. The red nucleus was completely replaced with a glial scar. In the right corpus Luysi (nucleus hypothalamicus) one perivascular devastated area was observed. The white matter of the inferior olives showed a moderate increase of neuroglia. The changes were chronic and of long standing; they were apparently based on vascular disease, the nature of which could not be determined. The involvement of the red nucleus was considered responsible for the choreic disturbances. According to Grünthal, the point of greatest interest was that progressive mental decay of a type ordinarily associated with diffuse damage to the cerebral cortex must be attributed in this case to circumscribed thalamic lesions. He speculates that the loss of parts of the thalamus which are closely connected with the frontal lobe can produce mental symptoms similar to those produced by involvement of the frontal lobe itself.

ROTHSCHILD, Worcester, Mass.

Diseases of the Spinal Cord

CHRONIC PAIN AS RESIDUAL OF POLIOMYELITIS. J. M. NIELSEN, Bull. Los Angeles Neurol. Soc. **10**:85 (Sept.-Dec.) 1945.

Nielsen observed a new syndrome of chronic pain as a residual of polyneuritic poliomyelitis in 15 cases in southern California. Reports of 6 cases are presented. The condition is characterized by neuritic and radicular pains, acroparesthesias

and a myotonic syndrome resembling myotonia congenita. After a subacute onset of pain, the course becomes chronic and continues for years, with exacerbations and remissions, possibly with a slow downward course. The sharp, shooting pains are almost exactly like those of tabes dorsalis. They affect not only the extremities but also the roots of the trunk and those supplying the trigeminal area. The pains differ from those of tabes in that they do not leave areas of hyperesthesia unless they become almost constant, and then late in the disease. Large areas are extremely sensitive to light touch but not to heavy pressure. All symptoms of destruction are extremely rare; the syndrome is almost exclusively irritative. The distribution of the gripping pains is that of the peripheral nerves. The acroparesthesia, the typical numbness of the hands and feet, is exactly like that of any sensory polyneuritis. The muscle spasms and myotonic syndrome do not seem related to any circulatory deficiency but, rather, appear to concern the muscles themselves or their nerve supply. But the anomalous condition exists that there is no tenderness of the nerve trunks or of the muscles in which the supposedly affected nerve endings are located unless the muscles are forced to contract many times by voluntary use. After such exercise there are much spontaneous pain in the group and a burning pain referred to the overlying skin. So far as is known, the syndrome does not respond to any treatment.

J. A. M. A.

DAMAGED INTERVERTEBRAL DISK: EARLY DIAGNOSIS AND TREATMENT. E. J. CRISP, Lancet **2**:422 (Oct. 6) 1945.

The lumbar intervertebral disks suffer trauma far oftener than is generally appreciated, but in the absence of crural pain or roentgenographic changes the resulting lesion is often mistaken for sacroilac strain or fibrositis. Crisp states that in the early diagnosis of injured intervertebral disk the most significant objective sign is the intense spasm of the lumbar muscles and the "tight" lumbar portion of the spine. Patients with a lesion of this type often suffer recurrent attacks of acute lumbago, indicative of further trauma, and the true nature of the condition may be recognized only when the disk ruptures completely.

Early diagnosis and treatment with immobilization will considerably reduce the incidence of sciatica. The author divides cases which escape diagnosis until after the onset of sciatic pain into two groups, depending on whether the annulus fibrosus is partially or completely ruptured. The first group may be recognized by a fixed lumbar lordosis; the second, by a fixed lumbar kyphosis. In both groups the lesion usually responds well to immobilization in a plaster spinal jacket. Surgical treatment may be reserved for cases in which the protrusion has not been reduced after a period of immobilization of three months, for cases of recurrent protrusion, and for cases in which severe pain persists long after the lumbar portion of the spine has reverted to its normal curve.

YASKIN, Camden, N. J.

PROTRUSION OF INTERVERTEBRAL DISK. B. H. BURNS and R. H. YOUNG, Lancet **2**:424 (Oct. 6) 1945.

Burns and Young conclude from their studies that recurrent backache in young adults is oftenest due to protrusion of an intervertebral disk. The earliest manifestation is backache, not sciatica. They regard what they call the orthopedic signs as being of the greatest importance in diagnosis of this condition. Not only is it possible to diagnose protrusion of the disk by the orthopedic signs alone, but in the early stages these are usually the only signs to be found. In many instances neurologic signs may make their appearance months, or occasionally years, after the onset of symptoms. The authors conclude that almost the only cause of sciatic scoliosis is protrusion of a disk. The most notable and constant characteristic of

protrusion of a disk is restriction of movement in the anteroposterior plane, whereas bending sidewise is free. The straight leg-raising test (Lasègue's sign) is of limited value. When the symptoms are slight and have never been severe, the authors recommend the patient to wear a belt or corset to restrict the movement of the lumbar portion of the spine. They do not favor the use of a plastic jacket, for it has proved a less comfortable, and no more effective, means of immobilization than a corset. Application of heat, massage, electrotherapy and injections of procaine may give temporary benefit in an attack by relieving spasm, but their effect, if any, is only transitory. The authors use a free exposure in operation because it gives easier access and a more comprehensive view of the lesion than the small interligamentous approach of a hemilaminectomy. The fifth lumbar and adjacent parts of the fourth lumbar and first sacral spinous processes are removed. The dura is then exposed by removing the lamina of the fifth lumbar vertebra and the adjacent ligamentum subflavum. The dura is not opened, and care is taken to avoid damage to the lateral vertebral joints. The authors conclude that precise localization can be achieved only by laminectomy. Myelographic studies and neurologic signs are of no help in localization. The use of contrast mediums and pneumograms has been abandoned.

Of 177 cases in which laminectomies were performed for suspected lesions of the disk, protrusions were found in 141. In 19 of the other cases intraspinal abnormalities capable of producing the symptoms were found. Of the 141 cases with proved lesions of the disk, immediate relief was obtained in 131, and the patients have remained free of symptoms.

YASKIN, Camden, N. J.

LUMBAGO: MECHANISM OF DURAL PAIN. J. CYRIAX, Lancet **2**:427 (Oct. 6) 1945.

Lumbago is defined as lumbar pain of sudden onset, severe enough to immobilize the patient for a short time. The pain is usually equal on the two sides of the back; occasionally it is asymmetric; strictly unilateral pain is uncommon. It is the author's opinion that the result of such an attack of pain is an internal derangement of a low lumbar intervertebral joint, as the result of a momentary posterior displacement of a movable piece of intra-articular fibrocartilage. The prolonged subsequent pain appears to be caused entirely by bruising of the dura mater. Lumbago provides the stage of symptoms due to a hypermobile or fragmented annulus fibrosus that is intermediate in degree between backache and sciatica. Defect of the fibrocartilaginous ring leading to pressure exerted on the dura mater via the posterior capsular ligaments is a common, but hitherto unrecognized, cause of backache. The best treatment for this condition appears to be a few days' rest in bed, followed, if symptoms persist, by epidural local anesthesia. The technic of anesthetization is as follows: The patient lies prone, and the cornua of the sacrum are identified. The skin between them is anesthetized with not more than 1 cc. of a 0.2 per cent solution of procaine hydrochloride. Too much solution introduced here obscures the landmarks. A lumbar puncture needle is inserted into the sacral hiatus and passed to a depth of 3 inches (7.5 cm.). The stylet is withdrawn and care taken to see that neither blood nor cerebrospinal fluid escapes. A 50 cc. syringe full of 0.5 per cent procaine hydrochloride in isotonic solution of sodium chloride is attached to the needle. The contents are slowly injected over a period of five to ten minutes.

Prophylaxis after recovery from an attack of lumbago consists in the maintenance of the lumbar lordosis. Radical cure, i. e., removal of the hypermobile or loose part of the annulus, presents such technical difficulties that the author has not recommended it until the stage of sciatica from root pressure has been reached.

YASKIN, Camden, N. J.

FAMILIAL POLIOMYELITIS: REPORT OF CASES. RAUL MAGGI, Rev. Asoc. méd. argent. **59**:302 (April 15) 1945.

Thirty-six of 600 cases (6 per cent) of poliomyelitis observed during the epidemic of 1942-1943 were familial, more than 1 case occurring in 17 families. In 15 families there were 2 cases each; in 2 families there were 3 cases each. In 8 instances the second case appeared simultaneously with the first; in 9 cases the second case came on from the third to the seventeenth day after the initial case in the family. In 2 cases no data were available on the interval between the primary and the secondary cases. Twenty-eight cases were of the paralytic and 8 of the nonparalytic form. Paralytic phenomena were more frequent in the initial cases.

N. SAVITSKY, New York.

ACUTE ANTERIOR POLIOMYELITIS COMPLICATING PREGNANCY. E. WAALER, Acta med. Scandinav. **123**:209, 1946.

Waaler reports 8 cases of poliomyelitis in pregnant women between 18 and 38 years of age. Seven cases occurred during an epidemic in Bergen, Norway, in 1941; the eighth case occurred in 1944. There were 2 fatalities. The author observed that poliomyelitis is no severer in pregnant women except during the last months of pregnancy, when there may be great discomfort if the respiratory muscles are involved. The prognosis is probably worse for the mother in late than in early pregnancy. The disease has little influence on pregnancy and labor. Labor is usually normal, and cesarean section is indicated only when paralysis embarrasses the respiration or when genitourinary complications are serious. It is likely that poliomyelitis is more frequent in pregnant women than in other adults, and the cases hitherto observed have been uniformly distributed with respect to the various stages of pregnancy. No evidence has been produced of intrauterine transmission of poliomyelitis. In this series of cases, the 5 live-form infants did not show any sign of paralysis or malformation. Follow-up investigation at the age of 3 years showed that all the children were well and that they had learned to walk at the usual age. In 1 case of stillbirth with spontaneous labor there was a history of previous stillbirth and no evidence that poliomyelitis was responsible. Microscopic examination of the nervous system of the fetuses of the 2 mothers who died in the sixth and the eighth month, of pregnancy, respectively, did not reveal any abnormality.

J. A. M. A.

Treatment, Neurosurgery

MODIFICATION OF THE ELECTRO-SHOCK CONVULSION BY SODIUM PENTOTHAL AND CURARE. MATTHEW BRODY, J. Nerv. & Ment. Dis. **102**:357 (Oct.) 1945.

While intravenous injection of sodium pentothal produces excellent narcosis, its relaxing effect is poor. The usefulness of the drug in conjunction with electroshock therapy is, therefore, limited, although it may be employed to produce a modified type of convulsion. Curare and sodium pentothal used together produce both narcosis and relaxation, thus reducing the risk of injury and obliterating the postconvulsive excitement in apprehensive, uncooperative or disturbed patients. Three hundred milligrams of freshly prepared sodium pentothal in 2.5 per cent solution is injected intravenously over a period of thirty seconds. With the same needle, but a different syringe, 0.45 mg. of curare ("intocostrin") per pound (0.5 Kg.) of body weight is injected slowly, over a period of a minute. The electrodes are applied, and four minutes after the injection is begun the current is applied.

Higher voltages or longer applications of current may be required. With this method, it is possible to treat extramurally patients who would otherwise require institutionalization.

CHODOFF, Washington, D. C.

INTRATHECAL AND ORAL VITAMIN THERAPY IN VARIOUS NEUROLOGIC DISORDERS. G. HEILBRUNN and N. HOFFENBERG, J. Nerv. & Ment. Dis. **102**:379 (Oct.) 1945.

Heilbrunn and Hoffenberg treated 15 patients with various disorders of the nervous system by the use of daily oral administration of 75 mg. of "ephynal acetate" (alpha tocopherol acetate), 6 mg. of thiamine hydrochloride, 3 mg. of riboflavin, 1.5 mg. of pyridoxine hydrochloride, 30 mg. of nicotinamide and 3 mg. of calcium pantothenate and weekly spinal injections of increasing doses (25 to 100 mg.) of crystalline thiamine hydrochloride. The treatment was continued for an average of nine and a half weeks. Of the 15 patients, 2, with a disorder diagnosed as tabes dorsalis, showed definite improvement, both subjectively and objectively. The other patients, with diseases which included Huntington's chorea, multiple sclerosis, lateral sclerosis, disseminated encephalomyelitis and postencephalitic parkinsonism, failed to show any favorable change. The authors believe that the improvement in the cases of tabes is probably significant and suggest that the lesions responsible for the condition may be due to a synergistic action of the spirochete and a latent nutritional deficiency.

CHODOFF, Washington, D. C.

ENDOLUMBAR PNEUMOENCEPHALOGRAPHY, SIMPLIFIED. JOSEPH H. GLOBUS and JOHN L. SIMON, J. Nerv. & Ment. Dis. **102**:412 (Oct.) 1945.

In order to make the procedure of pneumoencephalography less painful and shocking to the patient, the authors have devised a method by which the patient is kept lying on his side in bed, instead of being fastened in a chair in a sitting position. To obtain the necessary elevation of the patient's head to insure a rapid rise of the introduced air, the head of the bed is raised by placing the legs on tall shock blocks or on two chairs. This method has been employed in 28 cases, with satisfactory visualization in 22 cases, and without discomfort to the patient.

CHODOFF, Washington, D. C.

STREPTOMYCIN IN TUBERCULOUS MENINGITIS. R. E. COOKE, D. L. DUNPHY and F. G. BLAKE, Yale J. Biol. & Med. **18**:221 (Jan.) 1946.

Cooke and his co-workers report that a girl aged 1 year with tuberculous meningitis gave a history of intimate exposure to tuberculosis. A pulmonary lesion and a positive tuberculin test were demonstrated. The cerebrospinal fluid showed characteristic chemical and cytologic changes. Smears showed many acid-fast bacilli. Inoculation of guinea pigs produced the typical disease in five weeks, and the organisms were present in the lesions. Treatment with streptomycin began on the eighth hospital day. It was administered intramuscularly in an amount of 10,000 units in 1 cc. of isotonic solution of sodium chloride every two hours for the first week; 20,000 units was then given every two hours for thirty days. Because of lack of the drug, treatment was interrupted almost seven days. When therapy was resumed, the dosage of 20,000 units every two hours was continued for an additional twenty-nine days. The total amount of streptomycin given by intramuscular administration was 15,049,000 units, over a period of sixty-eight days. The initial daily amount of streptomycin given intrathecally was 1,000 units. This was gradually increased to 100,000 units by the fifteenth day of therapy. Two

hundred thousand units in 5 cc. of isotonic solution of sodium chloride was given intraventricularly every other day, beginning on the nineteenth day of treatment. Since the supply of streptomycin was becoming low, the amount was decreased to 100,000 units. There was a lapse of nine days in intrathecal administration, but treatment was resumed with 200,000 units every other day over a period of twenty-nine days. The total amount of intrathecal streptomycin was 4,951,000 units. The infant thus received a total of 20,000,000 units by the combined routes. The progression of tuberculous meningitis was arrested during treatment with streptomycin. The symptoms have decreased further since cessation of treatment. There is evidence that intramuscular and intrathecal administration of streptomycin favorably influenced the course of tuberculous meningitis in this case. This report is the first detailed account of the administration of streptomycin by the intrathecal route.

J. A. M. A.

PAINFUL PHANTOM LIMB TREATED BY HIGH CERVICAL CHORDOTOMY: REPORT OF 2 CASES. M. A. FALCONER and J. S. B. LINDSAY, Brit. J. Surg. **33**:301 (April) 1946.

Falconer and Lindsay report 2 cases of painful fantom in the upper limb of an army corporal, aged 27, and a war pensioner, aged 33, who were relieved by high cervical chordotomy performed by controlled graduated division, with local anesthesia. These 2 cases did not belong to the group in which relief was obtained by interruption of peripheral or sympathetic nerve pathways and in which pain impulses appear to arise in or around the neuromas of the divided nerves; they belonged to the other main group, in which painful impulses arise in the dorsal horn cells of the spinal cord and can be relieved only by section of the spinothalamic tract or by excision of the sensory cortex of the cerebrum. Infiltration of the appropriate peripheral or sympathetic pathways with a local anesthetic solution is a useful diagnostic procedure for distinguishing clinically between these two groups. When these diagnostic tests fail to give relief, section of the spinothalamic tract is suggested, and seems preferable to ablation of the sensory cortex because it does not destroy postural and other discriminative sensations in the stump, but only abstracts from it the sensation of pain and so renders the stump functionally useful for such purposes as carrying an artificial limb.

J. A. M. A.

PREFRONTAL LEUCOTOMY IN TREATMENT OF POST-ENCEPHALITIC CONDUCT DISORDER. F. T. THORPE, Brit. M. J. **1**:312 (March 2) 1946.

Thorpe describes 2 cases of adults aged 28 and 31, respectively, with post-encephalitic parkinsonism in which severe behavior disorders, present since childhood, were improved by means of bilateral prefrontal leukotomy. Complete amelioration of the aggressive and impulsive trends has been maintained in both cases for twenty-four and fourteen months, respectively.

In a study of 144 cases of severe disorders, Gibbs found that the fundamental cause of much of the abnormal behavior was "a state of tension or irritability of affect, driving [the patient] to periodic outbursts of impulsive conduct of characteristic simplicity, unpremeditated and unplanned." Surgical division of the fiber connections between the thalamus and the prefrontal area of the brain reduces this emotional tension.

ECHOLS, New Orleans.

TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS IN INFANTS BY OPENING THE LAMINA TERMINALIS. JEAN GUILLAUME and CHARLES RIBADEAU-DUMAS, Rev. neurol. **77**:173 (July-Aug.) 1945.

The authors report their experiences with the construction of an opening in the lamina terminalis, or the anterior wall of the third ventricle, in treatment of obstructive hydrocephalus. They report successful operations on 3 infants, 11, 6 and 3 months of age, respectively. The operations were performed with the use of local anesthesia. Two or three days before the operation ventricular drainage was carried out by means of puncture through the anterior fontanel. Such drainage facilitates adaptation of the brain to the altered hydrodynamic situation following the opening of the lamina terminalis. The authors suggest making a small puncture at first to allow the spinal fluid to flow slowly out of the ventricle; the opening is later enlarged. During the operation the ventricles are filled with Ringer's solution to prevent sudden collapse of the cerebral hemispheres. The operation in all 3 cases was successful so far as the enlargement of the head was concerned; in 1 case the head became smaller, and in another the child, who was blind, was able to see again.

N. SAVITSKY, New York.

Encephalography, Ventriculography, Roentgenography

DIAGNOSTIC VALUE OF PNEUMOENCEPHALOGRAPHY IN CASES OF DEMENTIA PARALYTICA. JEAN DELAY, P. NEVEU and P. L. DESCLAUX, Rev. neurol. **77**:179 (July-Aug.) 1945.

The authors analyze the value of pneumoencephalographic studies in 33 cases of dementia paralytica. One hundred to 220 cc. of spinal fluid was removed and replaced with air. Four types of roentgenograms were noted after insufflation of air. 1. In 15 cases the sulci were widened over the entire cortex; the ventricles were dilated; the frontal horns seemed somewhat rounded, and there was some loss of normal contour. Air was noted over the vertex in the region of the falx. 2. In 7 cases the ventricles were dilated, especially in the frontal region, but air was not noted over the cortex. The number of sulci which were dilated were few, especially in the frontal region. It is possible that this absence of air over the cortex was due to edema of the leptomeninges obliterating the spaces in that region. 3. In 2 cases there were disseminated spots of atrophy over the whole cortex. The lateral and third ventricles were not visualized; the cisterns at the base were not altered. 4. In 5 cases the ventricles were nearly normal. There were occasional slight widening of the frontal horns and slight filling of the sulci over the frontal lobes with air, indicating a moderate degree of atrophy in that region. The prognosis in the cases of type 1 was very poor; the patients did not recover. The prognosis was also poor in the cases of type 2. In some of these cases the disappearance of serous accumulations in the meninges was noted after malarial therapy. In cases of type 3 the results with therapy were also poor. In all 5 cases of type 4 the condition cleared up with treatment. No similar correlation was found in cases of juvenile dementia paralytica. The authors note a case of dementia paralytica with progressive hemiparesis and coma in which encephalographic studies showed a shift of the ventricular system; a subdural hematoma was observed at operation. The authors note that the frontal lobe was predominantly involved in all cases. They were unable to verify the observation of Hermann and Hernheiser (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **96**:730, 1925) that in cases of rementia paralytica with hallucinations the maximal changes in the pneumoencephalogram were noted in the region of the temporal lobes.

N. SAVITSKY, New York.

Obituaries

RICHARD HENRY HUTCHINGS, M.D.

1869-1947

Dr. Hutchings is dead. A man who for a generation was one of New York state's distinguished psychiatric figures is no more. While his example and inspirations are diminished, something of him will long remain.

Dr. Hutchings was born in 1869 and brought up in Georgia. He came to New York city in his early twenties, graduated from Bellevue Hospital Medical College in 1891 and served his internship on Blackwell's Island. He entered the service of the New York State Hospital in 1892 and continued in that service until he retired, in 1939. During his period of service, lasting forty-seven years, he was superintendent of the St. Lawrence State Hospital from 1900 to 1919 and superintendent of the Utica State Hospital from 1919 until his retirement, in 1939. He enlisted in the army during World War I and finished his federal service with the rank of major.

Many honors came to him, among them the presidency of the American Psychiatric Association in 1938. He was the head of the Oneida County Medical Association and a director of the National Committee for Mental Hygiene, made a survey of the State of Georgia at the request of its governor and in 1940 was given the honorary degree of Doctor of Science by Colgate University. During his later years he was the dean of New York psychiatrists and highly respected by his professional brothers.

Known to most of his associates as a person of limited physical stamina and handicapped by failing vision, men marveled at the acuteness of his mind and at his literary leanings. Early he saw that Freud had made a real contribution, and he combated, in his gentle way, the skepticisms of his contemporaries, never going too fast or too far, but always forward. When many men of his age were withdrawing, he published his famous "A Psychiatric Word Book" (Utica, N. Y.: State Hospitals Press), which, in its many editions, has found a place on the desks of psychiatrists, psychologists, psychiatric social workers and psychiatric nurses. For years he edited the *Psychiatric Quarterly,* wrote its editorials and saw it through the press, and up to the day of his death it was ever on his mind.

What an example Dr. Hutchings was! To his family he was a devoted husband and father, to his students an honored chief as well

as a professional guide and to his associates a trusted support. He could also be a considerable antagonist. Mentally alert, a southern gentleman in demeanor, he was a student to the last, with a deep interest in fine literature and the ability to use his resonant voice to express himself with studied dignified language. No one ever heard him use an uncouth word.

All of this went on for years in spite of slowly diminishing physical vigor, continued failing vision and episodes of acute ill health. With these handicaps who else would have struggled so manfully?

Richard Henry Hutchings died at his home in Clinton, N.Y., on Oct. 28, 1947 at the age of 78.

FREDERICK W. PARSON, M.D.

News and Comment

ANNOUNCEMENT OF POSTGRADUATE COURSES FOR QUALIFIED PHYSICIANS AT UNIVERSITY OF CALIFORNIA MEDICAL CENTER (1948)

The Faculty of the University of California Medical School, under the sponsorship of University Extension (Medical Extension), University of California, announce a full time postgraduate course in psychiatry and neurology, of twelve weeks, to begin about the middle of September 1948.

All these courses are available to veterans under the provisions of the G. I. Bill of Rights on presentation of a letter of eligibility and entitlement. Completed programs and details will be mailed on request to Stacy R. Mettier, M.D., Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22.

Book Reviews

Psychiatric Research. Papers read at the Dedication of the Laboratory for Biochemical Research, McLean Hospital, Waverley, Mass. By Cecil K. Drinker. M.D.; Jordi Folch, M.D.; Stanley Cobb, M.D.; Herbert S. Gasser, M.D.; Wilder Penfield, M.D., and Edward A. Strecker, M.D. Price, $2. Pp. 113. Cambridge, Mass.: Harvard University Press, 1947.

The six papers read at this dedication ceremony, held on May 17, 1946, are here fittingly recorded as the ninth number of the Harvard University Monographs in Medicine and Public Health. The review by Dr. Folch, the director of the new laboratory, entitled "Biochemical Problems Related to Psychiatry," is a masterful exposition of a series of anatomic, biochemical, metabolic and energy characteristics of the brain in a manner which leads directly to a host of problems capable of laboratory investigation. Dr. Penfield delivered an informative and provocative lecture on "Psychical Seizures," suggestive of the possibilities involved in the investigation of "brain biology." Dr. Cobb's lecture was in the form of a report on the work which had been done in the psychiatric wards of the Massachusetts General Hospital, dealing at some length with the investigations conducted there on the relation of neurocirculatory aesthenia and anxiety states. Drs. Drinker, Gasser and Strecker gave lectures on the history of McLean Hospital, the positivist's approach to psychiatric research and the "Psychobiology of Psychiatric Research," respectively.

Thus, the biochemical cerebral biologic, psychobiologic, psychosomatic and behavioristic viewpoints on psychiatric research were each represented in this symposium. Unfortunately, an exposition of what can be expected from the sociologic approach to research problems in psychiatry is missing.

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DECEMBER 1947

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second Class Matter Jan. 7, 1919, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

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